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March 14, 2005

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Art Unit: 1631
Examiner: M.P. Allen
Conf. No.: 6609

Re: U.S. Patent Application Serial No. 09/606,977 filed June 28, 2000
Inventor: Joseph R. BYRUM
Title: Nucleic Acid Molecules and Other Molecules Associated with Plants
Atty Dkt.: 16517.144

Sir:

Transmitted herewith for appropriate action by the U.S. Patent and Trademark Office (PTO) are the following documents:

1. Appellants' Brief, with attached Appendices A and B; and
2. Return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier.

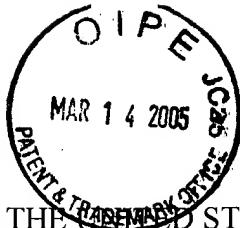
Authorization is hereby given to charge the statutory fee of \$500.00 for filing Appellants' Brief to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.144. A duplicate copy of this letter is enclosed.

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Appellants do not believe any additional fees are due in conjunction with this filing. However, if any fees are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.144. A duplicate copy of this letter is enclosed.

Sincerely,

Thomas E. Holsten (Reg. No. 46,098)
David R. Marsh (Reg. No. 41,408)

Enclosures



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:

Joseph R. BYRUM

Appln. No.: 09/606,977

Filed: June 28, 2000

Confirmation No.: 6609

Art Unit: 1631

Examiner: Marianne P. Allen

Atty. Docket: 16517.144

For: **Nucleic Acid Molecules and Other Molecules Associated with Plants**

APPELLANT'S BRIEF

Mail Stop Appeal Brief – Patents

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-captioned patent application. A Notice of Appeal was filed on January 14, 2005. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter.

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellant identifies the following judicial proceeding, which may have a bearing the Board's decision in the present Appeal. On May 27, 2004, the Real Party in Interest in the above-captioned matter filed an appeal to the United States Court of Appeals for the Federal Circuit ("Federal Circuit") from a decision by the Board in *In re Fisher*. (U.S.

Appln No. 09/619,643, B.P.A.I. Appeal No. 2002-2046, Fed. Cir. Case No. 04-1465). The Federal Circuit's decision in *In re Fisher* may have a bearing on the Board's decision with regard to at least one of the grounds of rejection in the present appeal. A copy of the Board's decision in Appeal No. 2002-2046 is attached hereto as Appendix B.

In addition, Appellant also identifies the following additional Board decisions which may have a bearing on the instant appeal: U.S. Appln. No. 09/654,617, B.P.A.I. Appeal No. 2003-1744; U.S. Appln. No. 09/620,392, B.P.A.I. Appeal No. 2003-1746; U.S. Appln. No. 09/540,232, B.P.A.I. Appeal No. 2003-1137; U.S. Appln. No. 09/440,687, B.P.A.I. Appeal No. 2003-1504; U.S. Appln. No. 09/565,240, B.P.A.I. Appeal No. 2003-1135; U.S. Appln. No. 09/540,215, B.P.A.I. Appeal No. 2003-0996; U.S. Appln. No. 09/552,087, B.P.A.I. Appeal No. 2004-1772; and U.S. Appln. No. 09/206,040, B.P.A.I. Appeal No. 2002-0078. Copies of the Board's decisions in these Appeals are also attached hereto in Appendix B.

Appellant also identifies the following pending appeals before the Board which may have a bearing on the instant appeal: U.S. Appln. No. 09/233,218, B.P.A.I. Appeal No. 2004-1725; U.S. Appln. No. 09/540,234, B.P.A.I. Appeal No. 2003-1073; U.S. Appln. No. 09/333,535, B.P.A.I. Appeal No. 2003-1939; U.S. Appln. No. 09/666,355, B.P.A.I. Appeal No. 2004-1034; U.S. Appln. No. 09/552,086, B.P.A.I. Appeal No. 2003-1074; U.S. Appln. No. 09/637,086, B.P.A.I. Appeal No. 2004-1273; U.S. Appln. No. 09/540,235, B.P.A.I. Appeal No. 2004-1275; U.S. Appln. No. 09/553,094, B.P.A.I. Appeal No. 2004-1406; U.S. Appln. No. 09/267,199, B.P.A.I. Appeal No. 2004-2136; U.S. Appln. No. 09/521,640, B.P.A.I. Appeal No. 2004-1666; U.S. Appln. No. 09/371,146, B.P.A.I. Appeal No. 2004-1272; U.S. Appln. No. 09/421,106, B.P.A.I.

Appeal No. 2004-1773; and U.S. Appln. No. 09/732,627, B.P.A.I. Appeal No. 2004-1480.¹

3. Status of Claims

Claims 1-7 and 20-24 are pending. Claims 8-19 were cancelled without prejudice to or disclaimer of the subject matter claimed therein in a response to office action filed January 7, 2003. Claims 1-7 and 20-24 stand finally rejected under 35 U.S.C. §§ 101 and 112, first paragraph and claims 23-24 also stand finally rejected under 35 U.S.C. § 102. Appellant appeals all of the rejections of claims 1-7 and 20-24.

4. Status of Amendments

Appellant has not filed any responses subsequent to Final Rejection in this case.

5. Summary of Claimed Subject Matter

The claimed subject matter is directed to a substantially purified nucleic acid molecule, the nucleic acid molecule capable of specifically hybridizing under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 2.0 X SSC at 50°C to a second nucleic acid molecule having a complete nucleic acid sequence of SEQ ID NO: 1 or complement thereof. Specification at page 10, lines 5-8 and page 1517, lines 3-6. The claimed subject matter is also directed to a substantially purified first nucleic acid molecule comprising a fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues; where the fragment nucleic acid sequence exhibits complete complementarity to a second nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 or complement thereof. Specification at page 15, line 17 through page 16, line 2. The claimed subject matter is

¹ Appellant notes that these appeals have been, or have been requested to be suspended pending a final determination in *In re Fisher*.

also directed to a substantially purified nucleic acid molecule, where the nucleic acid molecule comprises a nucleic acid sequence having between 90% and 100% sequence identity with a nucleic acid sequence of SEQ ID NO: 1 or complement thereof. Specification at page 1517, line 17 through page 1518, line 16. A copy of the claims on appeal is attached hereto as Appendix A.

6. Grounds of Rejection to be Reviewed on Appeal

The grounds of rejection to be reviewed in this Appeal are:

- (a) pending claims 2-3 and 6-7 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly containing new matter;
- (b) pending claims 1-7 and 20-24 stand rejected under 35 U.S.C. § 101 for allegedly being unsupported by a specific, substantial, and credible asserted utility or a well established utility;
- (b) pending claims 1-7 and 20-24 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because the claimed invention purportedly lacks utility; and
- (c) pending claims 23 and 24 stand rejected under 35 U.S.C. § 102, for alleged anticipation.

7. Argument

A. Summary of Appellant's Position

As the Supreme Court said in *Brenner v. Manson*, the “basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility...where specific benefit exists in currently available form.” 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Appellant has met their part of the bargain – they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public,

for example use to identify the presence or absence of a polymorphism in a population of maize plants. This benefit is specific, not vague or unknown, and it is a “real world” or substantial benefit. Because the claimed nucleic acid molecules provide at least these benefits, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed nucleic acid molecules for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Furthermore, Appellant has provided an adequate description of the claimed nucleic acid molecules that demonstrates Appellant’s possession of the claimed invention. Applicants have provided sufficient written description support in the specification and in the sequence listing such that a new matter rejection is improperly applied to claims 2-3 and 6-7. As such, Applicants have met the burden of written description and introduce no new matter by the inclusion of the noted claim language.

The claimed nucleic acid molecules are novel over the prior art. The claims are directed to nucleic acid molecules having between 90% and 100% sequence identity with a nucleic acid sequence of SEQ ID NO: 1 or complement thereof. The Examiner identifies a small nucleic acid fragment within the sequence of the cited reference. The Examiner has asserted an untenable interpretation of the claims to cover small fragments of the specifically claimed nucleic acid molecule, *i.e.*, molecules as short as 14 base pairs, and thus concludes that the claim is anticipated by the nucleic acid fragment in cited reference. Absent a teaching of each and every element of the claims, *i.e.*, nucleic acid molecules having the recited percent sequence identity with a nucleic acid sequence of SEQ ID NO: 1, or complements thereof, the reference cited by the Examiner does not anticipate the present claims.

B. The Specification Provides An Adequate Written Description of the Claimed Invention: No New Matter is Introduced

The adequacy of the written description of the claimed invention has been challenged by the Examiner because the inclusion of claim language “further comprising” in claims 2-3 and 6-7, added in the Amendment and Reply filed January 7, 2003, allegedly constitutes new matter.

The Examiner alleges that Applicants’ previous claim amendment “to indicate that the nucleic acid molecule according to claim 1 ‘further comprises’ an additional element” constitutes new matter. Office Action mailed March 25, 2004, page 2. The Examiner contends that the “amended claims would fairly encompass a sequence fully containing SEQ ID NO: 1 with an additional and unrelated microsatellite sequence (claim 2), with an additional and unrelated region containing a single nucleotide polymorphism (claim 3), and with an additional and unrelated promoter or partial promoter region (claim 6).” Final Action at 2-3. The Examiner goes on to argue that she “has only been able to find contemplation of where SEQ ID NO: 1 or a fragment thereof” contains these characteristics. *Id.*

In order to comply with the written description requirement of 35 U.S.C. §112, Applicants must ensure that each portion of a claim is “expressly, implicitly, or inherently supported in the originally filed disclosure.” MPEP §2163.05 at 2100-75; *Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The analysis for determining whether amended claim language constitutes ‘new matter’ “depends on the facts of the case: the nature of the disclosure, the state of the art, and the nature of the added matter. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 24 USPQ2d 1401 (Fed. Cir. 1992). Nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 1 or its complement are clearly present in Appellant’s disclosure as filed. See SEQ ID NO: 1 in the sequence listing. For example, Appellant’s specification contemplates nucleic acid molecules comprising SEQ ID NO: 1 or complements thereof combined with

other nucleic acid sequences, for example in DNA constructs (*See e.g.*, specification at page 1578 line 13 through page 1586 line 22) and in BAC constructs (*See, e.g.*, Specification at page 1606, line 11 through page 1612, line 17 and Table A). Accordingly, one of skill in the art can envision a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 or complements thereof combined with other nucleic acid sequences, for example, a microsatellite sequence, based on Appellant's disclosure.

In contrast, the Examiner has cited to one sentence of Appellant's disclosure for the proposition that SEQ ID NO: 1 is required to contain these elements. Final Office Action at pages 2-3. It is well-settled that the description of a claimed invention need not be in *ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972). Thus, the Examiner has not met the burden to impose a written description rejection of claims 2-3 and 6-7. ("[t]he Examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims.") *Wertheim*, 541 F.2d at 263, 191 U.S.P.Q. at 97, M.P.E.P. §2167.04 at 2100-73.

Moreover, the Examiner appears to be attempting to limit the claims to a particular aspect disclosed in the specification. In particular, the Examiner argues that the sentence bridging pages 1518 and 1519 in the specification shows the "intent of the specification" to be "that SEQ ID NO: 1 itself contains a microsatellite sequence." Office Action mailed March 25, 2004 at page 3. The Examiner argues that "[i]n the embodiment where the nucleic acid molecule of [original] claim 1 is the complete sequence of SEQ ID NO: 1, original claim 2 is interpreted to mean that SEQ ID NO: 1 itself contains a microsatellite sequence." *Id.* The Examiner goes on to argue that

“[o]riginal claim 2 is not interpreted to mean that a microsatellite sequence in addition to SEQ ID NO: 1 is present in the nucleic acid molecule.” *Id.* Original claim one is directed to “[a] substantially purified nucleic acid molecule, said nucleic acid molecule capable of specifically hybridizing to a second nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 82359 or complement or fragment thereof.” Original claim 2 recites “[t]he substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule comprises a microsatellite sequence.” The Examiner refers to the sentence bridging pages 1518 to 1519 and infers that the intent of the specification is that only the nucleic acid sequence comprised within the nucleic acid molecule of claim 1 can contain the microsatellite sequence. This is incorrect. Claims should not be limited to a single aspect disclosed in the specification. *See, Gentry Gallery, Inc. v. Berkline Corp.* 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998).

Moreover, the Examiner’s interpretation of the claims to require the characteristic, for example, a microsatellite sequence, be contained within SEQ ID NO: 1 is incorrect. Claim 1 as originally filed recites “a substantially purified nucleic acid molecule, said nucleic acid molecule capable of specifically hybridizing to a second nucleic acid molecule having a nucleic acid sequence... of SEQ ID NO: 1...” or complement thereof. Specification, page 1613, lines 2-5. Nowhere in claim 1 or its dependents was it ever recited that the additional elements must be or are contained within SEQ ID NO: 1. It is well-established law that use of the transitional term “comprising” or “having” leaves the claims “open for the inclusion of unspecified ingredients even in major amounts.” *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986). The very nature of “unspecified ingredients” is that they are not specified or described.

The Examiner attempts to turn the legal meaning of “comprising” on its head. In addition, the term “comprising” is defined by Section 2111.03 of the M.P.E.P. as synonymous with “including,” “containing,” or “characterized by,” and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. *See Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 U.S.P.Q.2d 1608, 1613 (Fed. Cir. 1997); *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1573, 43 U.S.P.Q.2d 1398, 1410 (Fed. Cir. 1997). Because claims 2-3 and 6-7 as originally filed were “comprising” claims, they did not exclude the possibility of further comprising the additional elements. Contrary to the Examiner’s assertion, the additional elements of each of these claims is not required to be found within SEQ ID NO: 1 or its complement, but rather may be found in a nucleic acid molecule that hybridizes to SEQ ID NO: 1 or its complement under the recited conditions. The Examiner’s interpretation is incorrect and unsupported by the law and the language of the claims as originally filed.

As such, written description of the claimed invention as amended has been satisfied, and inclusion of claim language “further comprises” in claims 2-3 and 6-7 does not constitute new matter. In light of all of the arguments above, claims 2-3 and 6-7 are supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112, and the rejection should be reversed.

C. The Claimed Nucleic Acids Have Legal Utility

Claims 1-7 and 20-14 stand rejected under 35 U.S.C. § 101 as allegedly lacking patentable utility “because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility. Final Action, at page 3.²

² Appellant notes that the Examiner indicates that this “rejection is maintained for reasons of record” and does not provide additional arguments in the Final Action.

Although the specification discloses numerous utilities the Examiner asserts that “[t]here does not appear to be a direct assertion as to how to use SEQ ID NO: 1.” Office Action mailed March 25, 2004 at page 3. The Examiner also asserts that “further research is required to use determine and confirm any of the uses set forth by the applicant for the claimed nucleotide sequences.” *Id.* at page 7.

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of “practical utility” developed by the courts after *Brenner v. Manson*. As the Examiner has acknowledged, the “threshold for utility is not high: An invention is ‘useful’ under section 101 if it is capable of providing some identifiable benefit.” *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide one identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) (“when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown”).

The courts have expressed a test for utility that hinges on whether an invention provides an “identifiable benefit.” *Juicy Whip*, 185 F.3d at 1366, 51 USPQ.2d at 1702. For analytical purposes, the requirement for an “identifiable benefit” may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or “substantial” benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be “totally incapable of achieving a useful result,” *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Appellant has asserted throughout the specification that the claimed nucleic acid molecules provide identifiable benefits, for example use to identify the presence or absence of a polymorphism, and use as a marker. *See, e.g.*, specification at page 1563, line 8 through page 1571, line 5 and page 1518, line 20 through page 1525, line 21. Either of these utilities described alone is enough to satisfy Section 101. Because Appellant need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

(1) The Claimed Nucleic Acid Molecules Provide A Specific Benefit, *i.e.*, They Have Specific Utility

Appellant has demonstrated that the claimed nucleic acid molecules are themselves useful for utilities disclosed in the specification, *e.g.*, to detect the presence or absence of polymorphisms. *See, e.g.*, specification at page 1563, line 8 through page 1571, line 5. The specification also discloses additional utilities for the claimed nucleic acid molecules, including, for example, use of the claimed nucleic acid molecules to measure gene expression in a sample,³ and use as molecular markers.⁴ *See e.g.*, specification at page 1571, line 13 through page 1572, line 11 and page 1546, line 16 through page 1571, line 5.

³ It is standard practice to screen populations of nucleic acids with sequences, often attached to a microarray, without characterizing each and every target mRNA. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. For example, such information is useful to detect expression changes in traits of interest.

⁴ One can use the claimed nucleic acid molecules to determine location of a corresponding DNA sequence on a physical map or genetic map location without knowing anything beyond the claimed sequence. The use of molecular markers is a practical activity in the development of nutritionally enhanced or agriculturally enhanced crops. Such markers are useful in, for example, genetic mapping or linkage analysis, marker-assisted breeding, physical genome mapping, transgenic crop production, crop monitoring diagnostics, and gene identification and isolation. As more markers are identified, genetic maps will become more detailed and it will be easier for plant breeders to breed for particular traits.

(a) Identifying the Presence or Absence of a Polymorphism

One of the utilities disclosed in the specification is use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism. Specification at page 1563, line 8 through page 1571, line 5. The Examiner argues that this utility, like many of the asserted utilities, is not specific or substantial, *see, e.g.*, Final Action at page 3, but does not provide any support (legal or factual) for the proposition that detection of polymorphisms using the claimed nucleic acid molecules is not a legal utility.

Many of the disclosed utilities in this case, including the detection of polymorphisms, are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell, or organism. The Examiner denigrates such utilities by asserting that these utilities are not useful because it would require further research to use the claimed nucleic acid molecules “to detect the presence and/or absence or identity of polymorphisms, as hybridization probes for expression profiling, as antisense inhibitors … to screen compounds such as herbicides, to measure the level of mRNA in a sample, and as a molecular marker.” Office Action mailed March 25, 2004, at page 6. However, the fact that, *e.g.*, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such “tools” have legal utility. “Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds).” MPEP § 2107.01 at page 2100-33.

Use of the claimed nucleic acid molecules to detect the presence or absence of polymorphisms is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas

chromatograph itself. Information has been obtained about the gas.⁵ Likewise, the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usefully demonstrates that the two (or more) populations being compared share a common genetic heritage.

The claimed nucleic acid molecules have been asserted to work for a specific, *i.e.*, not vague or unknown benefit, to identify the presence or absence of a polymorphism. This benefit is immediately realized directly from the use of the claimed nucleic acids, not from the use of other molecules. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Probes for Other Molecules or Source for Primers

Other uses for the claimed nucleic acid molecules are as probes for other molecules or as a source of primers. The Examiner again suggests that these uses are not legal utilities because the disclosed utilities require further research to search for a specific and substantial utility. Office Action mailed March 25, 2004 at pages 4-7. This is not correct. The specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules from other cereals, such as rice, sorghum, and wheat.⁶ Specification at page 1560, line 1 through page 1563, line 7. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and thus has not met the burden of proof required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560,

⁵ For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled “Chlorine Specific Gas Chromatographic Detector.”

⁶ Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Appellant to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed nucleic acid molecules.

1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

One illustrative example of a molecule that can be isolated using a claimed nucleic acid molecule is a gene linked to the claimed nucleic acid molecule. Applicants have specifically disclosed that one use of the claimed nucleic acid molecules is to initiate a chromosome walk. Specification at page 1554, line 10 through page 1555, line 3. The Examiner denigrates that utility by suggesting that it is not specific because “any EST⁷ would serve [this] purpose.” Office Action mailed March 25, 2004 at page 14. This is not correct. The claimed nucleic acid molecules are particularly useful, for example, to identify markers and isolate genes in maize plants. *See, e.g.*, specification at page 1546, line 16 through page 1559, line 23 and page 1606, *et seq* (Examples 1-2).

In short, the Examiner suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose, *e.g.*, chromosome walks. That position is wrong as a matter of law - there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) (“An invention need not be the best or the only way to accomplish a certain result...”). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading “into the patent laws limitations and conditions which the legislature has not expressed,” a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196

⁷ Appellant notes that SEQ ID NO: 1 has been referred to several times during prosecution as an EST. However, SEQ ID NO: 1 was obtained from a BAC clone containing maize genomic DNA, *See, e.g.*, Example 1, and therefore any reference to SEQ ID NO: 1 as an EST is incorrect.

(1980), quoting *United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not “specific” to the claimed nucleic acid molecules. The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate genes in maize plants. *See, e.g.*, specification at page 1546, line 16 through page 1559, line 23. A random nucleic acid molecule does not provide an equally good starting point to isolate such genes. Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules. An invention may be “less effective than existing devices but nevertheless meet the statutory criteria for patentability.” *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the claimed nucleic acid molecules could not be so used. Accordingly, the assertion of this utility as a probe for other molecules or as a source of primers satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

(2) The Claimed Nucleic Acid Molecules Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Final Action also asserts that the disclosed uses are legally insufficient because they are not “substantial” utilities. Final Action at page 3. The touchstone of “substantial” utility is “real world” or “practical utility.” *See, e.g.*, *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). “‘Practical utility’ is a shorthand way of attributing ‘real world’ value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public.” *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A.

1980) (“tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use”).⁸

There can be no question that one skilled in the art can use the claimed nucleic acid molecules in a manner which provides an immediate benefit to the public, for example to detect the presence or absence of polymorphisms. The detection of polymorphisms provides an immediate benefit to the public because, *e.g.*, it enables a plant breeder to determine the distribution of parental genetic material in the progeny of a cross. This information about a plant’s genetic profile, like the information about a compound’s pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

Quite apart from the detection of polymorphisms, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed “real world” value to such nucleic acid molecules. The utility of nucleic acid sequences is not merely an academic issue; the real world value of these constructs is self-evident from the growth of a multi-million dollar industry in the United States premised on their usefulness. Like fermentation processes involving bacteria, nucleic acid sequences and nucleic acid molecules with nucleic acid sequences are “industrial product[s] used in an industrial process – a useful or technical art if there ever was one.” *In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The market participants for nucleic acid sequence products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to pay for useless inventions. *Cf. Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983) (“People rarely, if ever, appropriate useless inventions”). Quite

⁸ *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

simply, the commercial value of these products is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

(3) The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered “credible” by a person of ordinary skill in the art. MPEP § 2107 at 2100-29. Cases in which utility was found not to be credible are rare, and usually involve “hare-brained” utilities.⁹ A challenge to the credibility of a utility is essentially a challenge directed to operability, and such a challenge must be supported by a clear statement of “factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability.” *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107.02 at 2100-41.

Appellant has explicitly identified specific and substantial utilities in the specification. “To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result.” *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d

⁹ Examples of incredible utilities are given in MPEP § 2107.01 at page 2100-34, and include:

an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on “flapping or flutter function” (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). To date, the Examiner has provided no evidence that the claimed nucleic acid molecules will not work for the disclosed utilities. Unless and until the Examiner can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

In view of the above, Appellant contends that the claimed nucleic acid molecules are supported by specific and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection of claims 1-7 and 20-24 under 35 U.S.C. §101 is improper and should be reversed.

D. The Claimed Nucleic Acids Are Enabled by the Specification

The enablement of the claimed nucleic acid molecules has been challenged. Pending claims 1-7 and 20-24 stand rejected as not enabled by the specification, because the claimed nucleic acid molecules allegedly lack utility and therefore cannot be enabled, for the reasons of record. Final Action at page 4. This rejection is erroneous and has been overcome by the arguments stated above regarding utility because it is well-established law that “the enablement requirement is met if the description enables any mode of making and using the invention.” *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), quoting *Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. See *In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) (“pure conjecture” does not substantiate rejection for lack of enablement).

E. The Claimed Nucleic Acid Molecules Are Novel

The novelty of the claimed invention has been challenged by the Examiner under 35 U.S.C. §102(a) because claims 23-24 are allegedly anticipated by Tikhonov *et al.* in view of GenBank Accession No. AF123535. Final Action at page 4. “It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention.” *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Further, “an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device.” *In re Donohue*, 766 F.2d 531, 226 U.S.P.Q. 619 (Fed. Cir. 1985). Nothing in the cited reference discloses the claimed nucleic acid molecules.

The Final Action alleges that “the language ‘a’ nucleic acid sequence embraces a subsequence of SEQ ID NO: 1 and the sequence of AF123535 [referred to in Tikhonov *et al.*] has 100% identity with at least the particular 14mer subsequence of Tikhonov *et al.* as set forth in the prior Office action.” Final Action at page 4. The Examiner has applied an untenable interpretation of pending claims 23 and 24 to cover small fragments of the specifically claimed nucleic acid molecules, *i.e.*, molecules as short as a 14mer, and thus concludes that the claims are anticipated by the cited reference. This is not correct.

Whatever else Tikhonov *et al.* as supported by GenBank Accession No. AF123535 disclose, they do not disclose or describe a nucleic acid sequence having the claimed percentage sequence identity with a nucleic acid sequence of SEQ ID NO: 1 or complement thereof. As such, the Examiner has failed to demonstrate that the references discloses a nucleic acid sequence having the recited percent sequence identity with a nucleic acid sequence of SEQ ID NO: 1 or a complement thereof and thus the rejection of pending claims 23 and 24 under 35 U.S.C. § 102 over Tikhonov *et al.* as supported by GenBank accession number AF123535 must be reversed.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,



Date: March 14, 2005

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APPENDIX A

Claims as Pending

1. A substantially purified nucleic acid molecule, said nucleic acid molecule capable of specifically hybridizing under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 2.0 X SSC at 50°C to a second nucleic acid molecule having a complete nucleic acid sequence of SEQ ID NO: 1 or a complement thereof.
2. The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule further comprises a microsatellite sequence.
3. The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule further comprises a region having a single nucleotide polymorphism.
4. The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1 or a complement thereof.
5. The substantially purified nucleic acid molecule according to claim 4, wherein said nucleic acid molecule further comprises a bacterial ORI site.
6. The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule further comprises a promoter or partial promoter region.

7. The substantially purified nucleic acid molecule according to claim 6, wherein said promoter region comprises a CAAT *cis* element and a TATA *cis* element and an additional *cis* element.

Claims 8-19 (Cancelled)

20. The substantially purified nucleic acid molecule according to claim 4, wherein said nucleic acid molecule consists of a nucleic acid sequence of SEQ ID NO: 1 or a complement thereof.

21. A substantially purified first nucleic acid molecule comprising a fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues; wherein said fragment nucleic acid sequence exhibits complete complementarity to a second nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 or complement thereof.

22. The substantially purified first nucleic acid molecule according to claim 21, wherein said second nucleic acid molecule consists of a nucleic acid sequence of SEQ ID NO: 1 or a complement thereof.

23. A substantially purified nucleic acid molecule having between 90% and 100% sequence identity with a nucleic acid molecule of SEQ ID NO: 1 or complement thereof.

24. The substantially purified nucleic acid molecule of claim 23, wherein said substantially purified nucleic acid molecule has between 99% and 100% sequence identity with SEQ ID NO: 1 or complement thereof.



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APPENDIX B

Related Proceedings Appendix



The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 26

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte DAVID K. KOVALIC and JINGDONG LIU

Appeal No. 2003-1744
Application No. 09/654,617

HEARD: June 8, 2004

MAILED

JUN 30 2004

U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

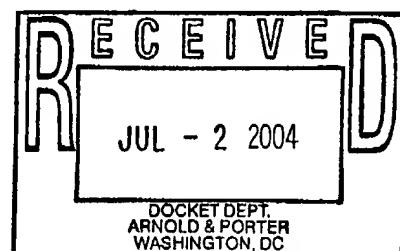
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 11-17. Claim 12 is illustrative of the subject matter on appeal and is reproduced below:

12. A substantially purified nucleic acid molecule comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782.

The examiner does not rely on a reference.



GROUNDS OF REJECTION

Claims 11-17 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. Claims 11-15 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention. We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph. Having disposed of all claims on appeal, we do not reach the written description rejection.

BACKGROUND

According to appellants' specification (page 1), "[t]he invention relates to nucleic acid sequences from plant cells, in particular, nucleic acid sequences from maize, teosinte, soybean, Arabidopsis, cotton, sorghum, rice and wheat." The specification also discloses (id., page 13), "[n]ucleic acid molecules of the present invention also include non-maize, non-sorghum, non-cotton and non-teosinte homologues. Preferred plant sources of homologues are selected from the group consisting of alfalfa, barley, Brassica, broccoli, cabbage, citrus, garlic, oat, oilseed rape, onion, canola, flax, an ornamental plant, pea, peanut, pepper, potato, rice, rye, strawberry, sugarcane, sugarbeet, tomato, poplar, pine, fir, eucalyptus, apple, lettuce, lentils, grape, banana, tea, turf grasses, sunflower, oil palm and Phaseolus." More particularly, appellants disclose "[t]he present invention provides a substantially purified nucleic acid molecule where the nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 463,173 or complements

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thereof or fragments of either;" or nucleic acid molecules that share between 90% to 100% sequence identity with one or more of the nucleic acid sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 463,173 or complements thereof or fragments of either. See e.g., specification, pages 3 and 11.

The original claims filed with the application were directed to all 463,173 nucleic acid sequences. On August 23, 2001 (Paper No. 6), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants to elect a single nucleic acid sequence for consideration on the merits. Paper No. 6, page 3. In response, appellants elected SEQ ID NO: 13,782.

CLAIM GROUPING

According to appellants (Brief, page 2), "[p]atentability of claims 11-17 is addressed together in sections 8.A through 8.D below." We understand appellants' statement to mean that claims 11-17 stand or fall together. Accordingly, we limit our discussion to representative independent claim 12. Claims 11 and 13-17 will stand or fall together with claim 12. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

CLAIM CONSTRUCTION

As set forth above, claim 12 on appeal is drawn to a substantially purified nucleic acid molecule comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782. According to

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appellants' specification (bridging paragraph, pages 8-9), the term "substantially purified"

refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the subject matter of claim 12 the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence set forth in SEQ ID NO: 13,782, but instead only allows for the addition of nucleotides or other molecules¹ at either end of the nucleotide sequence set forth in SEQ ID NO: 13,782. In this regard, we recognize, as does the examiner (Answer, page 4), the claim as written encompasses, inter alia, any full length gene, fusion construct, RNA or cDNA that contains about 50 nucleotide to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782.

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that comprises about 50 to about 100 nucleotide residues of the nucleic acid molecule defined

¹ According to appellants' specification (page 9), "agents of the present invention may be labeled with reagents that facilitate detection of the agent (e.g., fluorescent labels, ... chemical labels, ... [and] modified bases...."

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by the nucleotide sequence set forth in SEQ ID NO: 13,782 with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether the nucleic acid molecule of claim 12 possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695²,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

² In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1563-1564, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

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At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.³

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the

³ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that

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what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroid research and in the application of steroid materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there."

Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for

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the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use"

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that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a

practical utility for polypropylene at the time of the filing," but not yet there.

Ziegler, at 1203, 26 USPQ2d at 1605.

On this record, appellants' specification sets forth a number of utilities for the nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 463,173 including their use (1) as markers capable of detecting the level, pattern, occurrence or absence of a biological process, wherein the biochemical process is selected from among 55 different biochemical processes (specification, pages 3 and 16-19); (2) to express proteins from which antibodies can be made to immunoassay for the expressed protein or mimetics thereof (id. at pages 19-23); (3) in transforming or transfecting plants to either overexpress the encoded protein or block the expression of a target gene (id., pages 23-37, particularly page 34, last paragraph and page 35, third full paragraph); (4) to obtain other nucleic acid molecules from the same species, "including nucleic acid molecules that encode the complete coding sequence of a protein and promoters and flanking sequences of such molecules" (id., bridging paragraph, pages 37-38 and page 39); (5) to obtain nucleic acid homologues from other plants or organisms (id., pages 38-39); (6) to detect genetic polymorphisms (id., pages 39-44); (7) to monitor gene expression, e.g. through the use of a microarray (id., pages 44-51); (8) "to determine an attribute or feature (e.g. the presence or absence, location, correlation, etc.) of a molecule, cell, tissue or plant" (id., page 46-47); (9) "to identify a protein or fragment thereof that specifically binds to a nucleic acid molecule of the invention" (id., page 52).

We note, however, that the specification does not specifically disclose how to use a nucleic acid comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782, as set forth in claim 12.⁴ To the contrary, the specification describes the aforementioned utilities as applicable to all of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 463,173.

Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, *i.e.*, identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 40-44 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecule set forth in claim 12. To the contrary, according to appellants' specification (page 44, lines 7-8), "one or more [of the 463,173] nucleic acid molecule[s] or fragment[s] thereof of the invention can be used as a probe in accordance with the above-described polymorphic methods."

The specification does not explain why any of the 463,173 nucleic acid molecules disclosed in the specification, or more specifically a nucleic acid

⁴ On this record, the examiner finds "[t]here is no specific use particularly linked to the nucleic acids of the elected SEQ ID NO." Answer, page 3.

molecule comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 13,782 would in fact be useful in detecting polymorphisms.

Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that a nucleic acid by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleic acid, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, page 11), appellants' specification defines "polymorphism" as

"a variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species." It follows from this definition that if there is no "variation or difference in the sequence of the gene or its flanking regions" among "members of a species," then no polymorphism exists, i.e. a polymorphism is absent, in this region of the genome.

According to the examiner (Answer, page 10), "the presence or absence of the claimed nucleotide sequence in a sample (or polymorphisms thereof) has no meaning absent some association. Further experimentation is required to

determine what, if any, that meaning or association might be." In this regard, the examiner finds (Answer, page 11), appellants' specification "does not disclose whether the claimed nucleic acid molecules can, if fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves open the possibility that there may be no polymorphism to detect." According to the examiner (Answer, bridging paragraph, pages 11-12), "[t]he specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest." According to the examiner (Answer, page 13), "the specification fails to identify even one specific polymorphism that can be detected with the claimed nucleic acid molecule, the specification fails to show any specific correspondence between the disclosed general utility and the claimed subject matter, regardless of any specific application requiring detection of polymorphisms." Accordingly the examiner finds (id.), "using the claimed invention to first determine whether or not the claimed nucleic acid molecule can, in fact, detect a polymorphism is to determine whether or not the claimed invention has a utility that requires detecting a polymorphism, i.e. it is 'use testing' and not substantial."

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the nucleic acid is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the

gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.⁵

b. Probes or source of primers

Appellants assert that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to the nucleic acid set forth in claim 12. In the absence of such information, using the claimed molecule to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.⁶

Appellants also assert that the claimed nucleic acid molecule may be used in a "chromosome walk." Brief, page 8. According to appellants (Brief, page 9),

The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in Arabidopsis. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed

⁵ For the foregoing reasons, we disagree with appellants' assertion (Brief, page 3), claimed nucleic acid molecule provides "at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of Arabidopsis."

⁶ According to the examiner (Answer, page 14), "since further research is needed to determine what, if any, real world utility the 'other nucleic acid molecules' may have, the use of the claimed nucleic acid for obtaining the 'other nucleic acid molecules' falls short of a substantial utility."

nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

As we understand this argument, the claimed nucleic acid may be useful in searching for promoters that active in Arabidopsis. The specification, however, fails to demonstrate that the nucleic acid molecule set forth in claim 12 would be useful in obtaining a successful result from such a search. As set forth at page 39, lines 15-20 of appellants' specification,

The [463,173] nucleic acid molecules of the present invention may be used to isolate promoters of cell enhanced, cell specific, tissue enhanced, tissue specific, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 463,173 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid molecule of claim 12 to isolate promoters of cell enhanced, cell specific, tissue enhanced, tissue specific, developmentally or environmentally regulated expression profiles.

According to the examiner (Answer, page 15), "the specification fails to disclose any characteristics of the corresponding promoter, or any other promoter within 'chromosome walking' distance; neither structural characteristics, by which the promoter might be identified, nor functional characteristics, by which a specific and substantial use for the promoter might be determined." By

way of example, the examiner argues (Answer, page 16), assume

a nucleotide sequence is identified during the chromosome walk as a putative promoter by sequence analysis, is then subcloned into operable linkage with a reporter gene and transfected into an appropriate cells, but found not to express the reporter gene in the cells. This result could mean the putative promoter: is not truly a promoter, i.e. a false positive; is not the corresponding promoter; or is incomplete, i.e. lacked additional sequence elements required for promoter activity in the seed pod cells.

According to the examiner (Answer, page 9), appellants merely isolated the claimed nucleic acid molecule, “[t]hey have not tested, evaluated, or calibrated the claimed nucleotide sequence for any particular use.”

We recognize appellants' argument (Brief, page 9), “[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).” While we agree with appellants' statement, we fail to see how it applies to appellants' claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be “effective” at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is “refined and developed” to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful

as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide or traits such as disease resistance." Brief, page 5. Specifically, appellants argue (*id.*) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Brief, bridging sentence, pages 5-6.

However, the examiner finds (Answer, page 6), further research is required to use of the claimed nucleic acid molecule's use to detect the presence and/or identity of polymorphisms, as hybridization probes for expression profiling,

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as antisense inhibitors by introduction of the claimed nucleic acid molecule into a plant or plant cell where the resulting cell or plant is to be used to screen compounds such as herbicides, to measure the level of mRNA in a sample, and as a molecular marker. In addition, the examiner finds (*id.*), that since targets are not disclosed in the specification, the use of the claimed nucleic acid molecule "as antisense inhibitors would require further experimentation to determine the target of inhibition." To the extent that appellants would argue that the claimed nucleic acid could be used in assays that measure the presence of a material that correlates to a predisposed disease condition, the examiner finds (Answer, page 7), "[t]he instant specification sets forth no such correlation for any condition."

As to the use of the claimed nucleic acid in microarrays (see e.g., Brief, page 6, n. 3), the examiner finds (Answer, page 7), "[a]ppellant is [sic] not claiming microarrays or collections of nucleotides and the specification does not associate the claimed sequence with any trait of interest." According to the examiner (Answer, page 8),

locating and measuring nucleic acid molecules within a sample is not a substantial use because it takes further research to determine any substantial use of the results of locating and measuring. The specification discloses no substantial uses of locating and measuring any nucleic acid molecule that does not consist or comprise SEQ ID NO: 13[.]782.

In addition, the examiner acknowledges appellants' assertion (Brief, page 5, n. 1), "[i]t is irrelevant whether the corresponding mRNA or polypeptide have utility because [a]pplicants are not relying on utility of the mRNA or polypeptide to

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establish utility of the claimed nucleic acid molecules." Answer, page 6.

Nevertheless, the examiner asserts (*id.*), "[t]he [B]rief does not dispute that no open reading frame (ORF), no encoded protein, nor any biological activity for any encoded protein has been disclosed for SEQ ID NO: 13[,]782."

As for non-asserted utilities, the examiner finds (Answer, bridging paragraph, pages 3-4), "[n]either the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the elected nucleic acid compound."

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. In regard to microarrays, we find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid molecule set forth in claim 12. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the specific information derived from a gene expression experiment would mean in the context of a nucleic acid molecule as set forth in claim 12.

To highlight the examiner's assertion (Answer, pages 7-8), suppose, for example, that a researcher found that expression of the nucleic acid molecule set forth in claim 12 was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the nucleic acid molecule of claim 12 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility

because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use the specific gene expression data in the context of the nucleic acid molecule of claim 12.

Assuming arguendo, that a generic gene expression assay - one based on monitoring expression of thousands of uncharacterized nucleic acids - would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of

patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecule set forth in claim 12 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 12 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 10. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 12 in such devices represents a substantial use.

Further, we understand appellants' position to be that a compound would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one

set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

Not only is appellants' proposed utility standard contrary to controlling case law, but there are reasons to expect that it would hurt – rather than help – the microarray industry. Under appellants' standard, any naturally occurring gene, and fragments thereof, would be held to have patentable utility based on its use in generating expression data. The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating the patent status of each oligonucleotide on the microarray. Not only that, but since appellants assert that their reasoning supports the utility of gene fragments, all of the subsequences of each of the genes or polypeptides would have to be checked to ensure that it was not the subject of someone else's patent.

For each of the genes (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons":⁷

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate

⁷ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," *Science*, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859).... To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101.

For the foregoing reasons we affirm the rejection of claim 12 under 35 U.S.C. § 101. As discussed supra, claims 11 and 13-17 fall together with claim 12.

Enablement

According to the examiner (Answer, page 4), "since the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), this rejection should be reversed for the same reasons set forth in their arguments regarding the rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 12 under the enablement provision of 35 U.S.C. § 112, first paragraph. As discussed supra, claims 11 and 13-17 fall together with claim 12.

Written description

Having disposed of all claims on appeal we do not reach the merits of the rejection under the written description provision of 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith
William F. Smith
Administrative Patent Judge

Donald E. Adams
Donald E. Adams
Administrative Patent Judge

Eric Grimes
Eric Grimes
Administrative Patent Judge

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Appeal No. 2003-1744
Application No. 09/654,617

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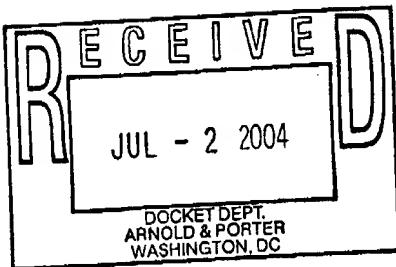
The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 35

UNITED STATES PATENT AND TRADEMARK OFFICE

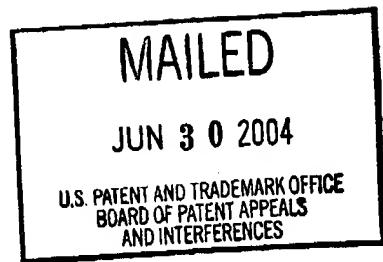
BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ANDREY A. BOUKHAROV,
YONGWEI CAO, DAVID K. KOVALIC,
JINGDONG LIU, JAMES McININCH,
and WEI WU



Appeal No. 2003-1746
Application No. 09/620,392

HEARD June 8, 2004



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.
GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-4, 6-9, and 16-20, all of the claims remaining. Claims 1 and 2 are representative and read as follows:

1. A substantially purified nucleic acid molecule having a nucleic acid sequence of SEQ ID NO:1 or complement thereof.
2. A substantially purified nucleic acid molecule comprising a fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues; wherein said fragment nucleic acid sequence exhibits complete complementarity to a second nucleic acid molecule having a nucleic acid sequence of SEQ ID NO:1 or complement thereof.

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The examiner does not rely on any prior art.

Claims 1-4, 6-9, and 16-20 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility.

Claims 1-4, 6-9, and 16-20 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description.¹

We affirm the utility rejections and reverse the description rejection.

Background

The subject matter of the present appeal is directed to "genomic DNA sequences from Oryza sativa (rice) plants." More specifically, the "invention provides a substantially purified nucleic acid molecule, the nucleic acid molecule capable of specifically hybridizing to a second nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:69652 or complements thereof or fragments of either."

According to the specification,

[a] subset of the nucleic acid molecules of the present invention includes nucleic acid molecules that are marker molecules. Another subset of the nucleic [acid] molecules of the present invention includes nucleic acid molecules that are promoters and/or regulatory elements. Another subset of the nucleic acid molecules of the present invention includes nucleic acid molecules that encode a gene or fragment thereof. Another subset of the nucleic acid molecules of the present invention encodes proteins or fragments of proteins.

Page 17. The specification provides no further guidance on which of the 69,652 disclosed sequences fall into each of these subsets.

¹ The examiner's statement of the rejection actually speaks in terms of lack of enablement. See the Examiner's Answer, page 5 (The claims "contain[] subject matter which lacks written description in the specification in such a way as to enable one skilled in the art . . . to make and/or use the invention."). The

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The originally filed claims encompassed all of the 69,652 disclosed sequences. See, e.g., original claim 1 (specification, page 55,578).² On June 18, 2001 (Paper No. 7), the examiner entered a restriction requirement into the record, requiring appellants to elect, *inter alia*, a single nucleotide sequence for examination on the merits. Paper No. 7, page 2. In response, Appellants elected SEQ ID NO:1. See Paper No. 8, received July 17, 2001.

The disclosure that relates specifically to SEQ ID NO:1 is found in the specification's Table 1 and reads as follows, in its entirety:

Seq No.	1	Seq. ID	OJ990503_31.9819.C2
Gene No.	1	Strand	-
Start	397	End	1864
Name	OJ990503_31.9819.C2.o1.gs	Method:	GENSCAN
Start	397	End	1238
GI	none	Score	.93
Exons	397..591, 879..1238		
Seq No.	1	Seq. ID	OJ990503_31.9819.C2
Gene No.	1	Strand	-
Start	397	End	1864
Name	OJ990503_31.9819.C2.o1.tm	Method:	TBLASTX:Maize
Start	1017	End	1864
GI	none	Score	150
Exons	1017..1250, 1018..1245, 1020..1247, 1243..1296, 1249..1296, 1377..1418, 1382..1420, 1532..1600, 1534..1596, 1706..1735, 1745..1864		

Page 104.

The specification sets forth a number of utilities for the claimed nucleic acid molecule which are characterized by the examiner as "[g]eneric to any rice nucleic acid

examiner's reasoning, however, explains the rejection in terms of lack of written description. We understand the rejection to be based on the written description requirement of § 112.

² The record is unclear as to precisely how many pages are in the specification. According to an error sheet generated by the USPTO's Office of Initial Patent Examination, the specification contains 68,885 pages; according to Appellants' page numbering, it contains only 55,580 pages. We have not attempted to resolve this discrepancy since it does not affect the issues on appeal.

sequences." Examiner's Answer, page 4. The examiner concluded that these uses do not establish patentable utility:

The claimed nucleic acids are not supported by a specific asserted utility because the disclosed uses of these nucleic acids are generally applicable to rice genomic nucleic acid. The specification states that the nucleic acid compounds are useful for gene mapping, marker assisted introgress[ion of traits, physical mapping, etc. (page 9 and 49). All these possible uses are generic to any rice nucleic acid sequences. Further, the claimed nucleic acids are not supported by a substantial utility. . . . Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds.

Examiner's Answer, pages 3-4.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See the Appeal Brief, pages 6-13. According to Appellants, "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example, the ability to identify the presence or absence of a polymorphism in a population of rice plants." Id., page 4. Furthermore, appellants assert, "[t]he specification discloses that the claimed nucleic acid molecules can be used . . . to isolate nucleic acid molecules of other plants and organisms." Id., page 9.

1. Claim construction

The claims stand or fall together. Appeal Brief, page 3. Claim 2 is the broadest claim on appeal and we will consider it as representative.

As set forth above, claim 2 is directed to a "substantially purified" nucleic acid molecule that comprises a "fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues"; where the 50-100 nucleotide sequence "exhibits complete complementarity to a second nucleic acid molecule having a nucleic acid sequence of SEQ ID NO:1" or its complement.

The specification defines "substantially purified" to mean

a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

Page 16, lines 12-18. As we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g., insertions or deletions) of the "fragment nucleic acid sequence" recited in the claim, but instead only allows for the addition of nucleotides or other molecules at either end of that sequence. Thus, claim 2 encompasses, inter alia, genes and fragments thereof, full or partial open reading frames, fusion constructs, and cDNAs.

Accordingly, we interpret claim 2 as directed to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that includes at least about 50 nucleotides that are completely complementary to a part of SEQ ID NO:1 or to the complement of a part of SEQ ID NO:1.

2. Utility

The starting point for determining whether the claimed nucleic acid molecules possess utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.³

³ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroid research and in the application of steroid materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the

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compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are.” Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. “There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of ‘useful in research’ or ‘useful as building blocks of value to the researcher’ was recognized, and clearly rejected, by the Supreme Court” in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. “In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was ‘plastic-like.’” Id. at 1203, 26 USPQ2d at 1605. “Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility.” Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. “[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there.” Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by

"marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy

§ 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal; i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We will focus on these asserted utilities first.

a. Polymorphisms

This utility is discussed at pages 57-64 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to SEQ ID NO:1. To the contrary, according to the specification, "[t]he [69,652] nucleic acid molecules of the present invention can be used to identify polymorphisms. In one embodiment, one or more of the nucleic acid molecules . . . may be employed as a marker nucleic acid molecule to identify . . . polymorphism(s)." Page 57. The specification does not explain why any particular one of the 69,652 nucleic acid molecules disclosed in the specification, or more specifically SEQ ID NO:1, would in fact be useful in detecting polymorphisms.

Rather, Appellants argue that "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." Appeal Brief, page 9. In other words, Appellants' position is that a rice genomic DNA by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleotide sequence, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains,

[a] "polymorphism" is a collective concept defined by at least two variants (or alleles) found within members of a species collectively. Thus, one detects the presence of a polymorphism by analyzing multiple members of the species, i.e. analyzing a population. . . . The specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. . . .

The specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphism that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest.

Examiner's Answer, pages 12-13. In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene represented by the claimed sequence has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line that defines "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms." Appeal Brief, page 9. That may be true, but it does not show the patentable utility of the claimed nucleic acids, because the nucleic acids isolated from other plants have no apparent, substantial use. Again, the present specification does not attribute any property in terms of plant trait or phenotype to SEQ ID NO:1. In the absence of such information, nucleic acids from other plants that hybridize to the claimed nucleic acids themselves lack substantial utility. Thus, the use of the claimed nucleic acids to isolate such nucleic acids does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Appeal Brief, pages 10-11. According to Appellants,

[t]he claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in Oryza sativa. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

Id., page 10. As we understand it, Appellants' argument is that the claimed nucleic acids may be useful in searching for promoters that are active in rice tissues.

The specification, however, fails to demonstrate that the nucleic acid represented by SEQ ID NO:1 would be useful in obtaining a successful result from such a search.

The specification states that "[a]nother class of agents of the present invention are nucleic acid molecules having promoter regions or partial promoter regions within SEQ ID NO:1 through SEQ ID NO:69652." Page 27.

Promoters . . . include, but are not limited to, oxygen responsive cis elements . . ., light regulatory elements . . ., elements responsive to gibberellin . . ., elements responsive to abscisic acid . . ., elements similar to abscisic acid responsive elements . . ., auxin responsive elements . . ., ethylene responsive cis elements . . ., sucrose responsive elements . . ., heat shock response elements . . ., Elicitor responsive elements . . ., drought responsive elements . . ., light-independent regulatory elements . . ., ACGT elements . . ., [and] prolamin box elements.

Pages 28-32.

The specification does not provide any expectation of successfully using any of the 69,652 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid of SEQ ID NO:1, to isolate any of the promoters exhaustively listed in the specification, or any other promoter. Even if SEQ ID NO:1 represents a gene that is expressed in rice tissue, the specification provides no characterization of its expression (e.g., amount expressed, timing of expression, tissues in which or conditions under which it is expressed) that would suggest a utility for its putative promoter.

It is true, as Appellants argue, that “[a]n invention may be ‘less effective than existing devices but nevertheless meet the statutory criteria for patentability.’” Appeal Brief, page 11. However, with Appellants’ claimed invention, there is no evidence or expectation that the claimed nucleic acid molecules would be “effective” at all. An invention does not have utility sufficient to satisfy § 101 until it is “refined and developed” to the point of providing a specific benefit in currently available form. See Brenner, 383 U.S. at 534, 148 USPQ at 695.

Appellants argue that the claimed nucleotide sequences are no less useful just because other nucleic acids can also be used to isolate promoters. See the Appeal Brief, page 10: “[T]he Examiner suggests that the asserted utilities are legally

insufficient simply because other molecules can be used for the same purpose. This position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law.”

This argument is not persuasive. Appellants have not been asked to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, Appellants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is “refined and developed” to the point of providing a specific benefit in currently available form.).

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics.

On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

Here, Appellants argue that asserted "chromosome walking" utility would support patentability even if the claimed nucleic acid molecule was less useful for this purpose than a totally random nucleotide sequence. Appeal Brief, page 10 ("[E]ven if a random nucleic acid provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules."). Clearly, the asserted utility is not based on the specific properties of the claimed nucleic acid molecules.

c. Other arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules, including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Appeal Brief, page 6 (footnote omitted). Specifically, Appellants argue (*id.*) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which, they assert, has a "legally sufficient utility." *Id.*

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portions of the specification cited in support of this argument (pages 69 and 86-88) indicate that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in either expression of the protein or suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to

be used is uncharacterized as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular markers. Appeal Brief, page 7. In regard to microarrays, Appellants argue (*id.*, n.3) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that this asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in SEQ ID NO:1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification provides no guidance regarding what the SEQ ID NO:1-specific information derived from a gene expression experiment would mean. As the examiner points out, "further experimentation is required to identify a 'real world use.' . . . A positive result to such a screen requires further experimentation to determine what, if anything, such a change means." Examiner's Answer, pages 8-9.

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO:1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be

able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO:1 expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), or the degree of increase? The specification provides no guidance as to how to interpret the results that might be seen using SEQ ID NO:1 in a gene expression assay.

In effect, Appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, Appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, based on their use in gene expression assays, because the specification does not disclose how to use gene expression data pertaining to SEQ ID NO:1.

In addition, assuming arguendo that a generic gene expression assay—one based on monitoring expression of a collection of uncharacterized nucleic acids—would

provide a useful tool for, e.g., drug discovery, it does not follow that each of the nucleic acids in the assay necessarily has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture.

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands, even if the thousands of data points collectively are useful, does not meet this standard.

We also conclude that § 101's utility requirement is not satisfied by Appellants' assertion that the claimed nucleic acid molecules are useful as molecular markers or probes. Again, using one of the claimed nucleic acids as a molecular marker or probe to hybridize to part of a rice chromosome merely generates a single, uncharacterized data point that is useful only when combined with thousands of other data points. For the reasons discussed above in regard to gene expression assays, such uses do not represent "substantial" utility, as required by Brenner.

Appellants argue that ESTs (and presumably other uncharacterized nucleic acids – the claims on appeal are not directed to ESTs) have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Appeal Brief, page 12. Since Appellants fail to provide any

suggestion of which use of ESTs this industry is premised on, we can only assume that Appellants are referring to the potential usefulness of EST databases, clone sets, or microarrays. The claims on appeal, however, are not directed to EST databases, clone sets, or microarrays, but to individual, uncharacterized nucleic acids. Again, we do not agree that the one data point which may be provided by using the uncharacterized nucleic acid molecules of the claims in such devices represents a substantial use.

In addition, it is reasonable to expect that the rule Appellants proffer – that uncharacterized nucleic acids are individually patentable because they are useful in gene expression assays – would hurt, rather than help, what they characterize as a “multi-million dollar industry in the United States premised on the usefulness of ESTs.” Under Appellants’ standard, any uncharacterized nucleic acid from most (if not all) organisms would be held to have patentable utility based on its use in generating gene expression data.⁴ The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating all of the DNA sequences on the microarray to ensure that they were not the subject of someone else’s patent.

For each of the DNAs that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each

⁴ We can take judicial notice of the fact that organisms are of interest for many different reasons, such that gene expression assays could conceivably be used in their research. Humans, of course, are of interest in medical research. Other organisms are of interest to researchers because they have been historically well-studied (e.g., yeast, Arabidopsis, Drosophila), or because they are used as animal models for testing pharmaceuticals (e.g., mice, chimpanzees, rabbits), or because they are commercially valuable (e.g., pigs, corn, tomatoes), or because they are pests (e.g., Fusarium, ragweed, corn borers, zebra mussels), or because they are pathogens (e.g., Candida, various bacteria, tapeworms).

new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons":⁵

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859). . . . To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. We therefore affirm the rejection of claim 2 under 35 U.S.C. § 101.

Claims 1, 3, 4, 6-9, and 16-20 fall with claim 2.

⁵ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

3. Enablement

The examiner rejected claims 1-4, 6-9, and 16-20 under 35 U.S.C. § 112, first paragraph, on the basis that "since the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." Examiner's Answer, page 4. This rejection is simply a corollary of the finding of lack of utility.

Appellants argue that "[t]his rejection . . . has been overcome by the arguments stated above regarding utility." Appeal Brief, page 14. We do not agree that Appellants' arguments overcome the rejection for lack of utility. Thus, our conclusion with respect to the § 101 issue also applies to the nonenablement rejection. On this basis we affirm the rejection of claims 1-4, 6-9, and 16-20 under the enablement provision of 35 U.S.C. § 112, first paragraph.

4. Written description

The examiner rejected claims 1-4, 6-9, and 16-20 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, reasoning that

[c]laims 1-4, 6-9, and 16-20 are directed to nucleic acids comprising . . . SEQ ID NO:1, or fragments thereof. . . . [G]iven the broad scope of the claims, they are drawn to a genus: any polynucleotide or nucleic acid that minimally contains the sequence of the claimed SEQ ID NO, or a fragment thereof, including any full length gene which contains the sequence. . . . Since the claimed genus encompasses species yet to be discovered, the mere disclosure of a species: sequence of the claimed SEQ ID NO, does not provide an adequate description of the claimed genus. . . . With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotide.

Examiner's Answer, page 5.

As we understand it, the basis of the examiner's rejection is that because of the transitional phrase "comprising", the claims encompass a large genus of nucleic acid molecules which are not adequately described by SEQ ID NO:1. See the Examiner's Answer, pages 18-20. Apparently, the examiner is of the opinion that the claimed invention should be limited to the nucleic acid molecules set forth in SEQ ID NO:1.

In response, Appellants argue that "[t]he fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences . . . does not mean that Applicants were any less in possession of the claimed nucleic acid molecules." Appeal Brief, pages 15-16.

We have interpreted claim 2 to allow for the addition of nucleotides or other molecules at either end of the recited nucleotide sequences, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence SEQ ID NO:1. See pages 4-5, supra. We agree with Appellants that the claims, as we have interpreted them, are supported by an adequate written description in the specification. The fact that the claimed nucleic acid molecules may have other molecules attached to either or both of their 5' or 3' ends does not diminish Appellants' adequate written description of the nucleic acids molecules with at least part of the sequence set forth in SEQ ID NO:1, as claimed.

Accordingly, we reverse the rejection of claims 1-4, 6-9, and 16-20 for lack of adequate written description.

Summary

Although we reverse the examiner's rejection for lack of adequate written description, we affirm the rejection of claims 1-4, 6-9, and 16-20 for lack of patentable utility.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith
WILLIAM F. SMITH)
Administrative Patent Judge)

Donald E. Adams)
DONALD E. ADAMS)
Administrative Patent Judge)
BOARD OF PATENT

Eric Grimes)
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APPEALS AND
INTERFERENCES

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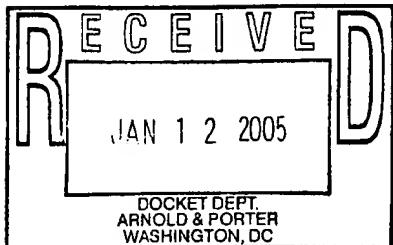
The opinion support of the decision being entered today as not written for publication and is not binding precedent of the Board.



UNITED STATES PATENT AND TRADEMARK OFFICE

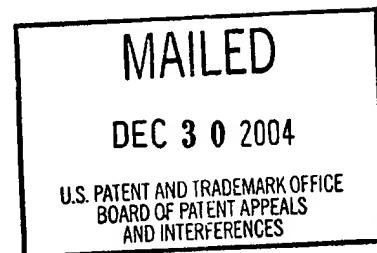
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JOSEPH R. BYRUM



Appeal No. 2004-1772
Application No. 09/552,087

ON BRIEF



Before WILLIAM F. SMITH, ADAMS, and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 3, 5-7, 9, 10, and 12-20, which are all the claims pending in the application.

Claims 3, 7 and 12 are illustrative of the subject matter on appeal and are reproduced below:

3. A transformed plant cell having a nucleic acid molecule which comprises:
 - (A) an exogenous promoter region which functions in said cell to cause the production of a mRNA molecule, wherein said promoter nucleic acid molecule comprises SEQ ID N0: 1 or a complement thereof; which is linked to
 - (B) a structural nucleic acid molecule encoding a protein or peptide; which is linked to

(C) a 3' non-translated sequence that functions in said cell to cause termination of transcription and addition of polyadenylated ribonucleotides to a 3' end of said mRNA molecule.

7. A transformed plant having a nucleic acid molecule which comprises:
 - (A) an exogenous promoter region which functions in a plant cell to cause the production of a mRNA molecule, wherein said promoter nucleic acid molecule comprises SEQ ID NO: 1, or a complement thereof; which is linked to
 - (B) a structural nucleic acid molecule encoding a protein or peptide; which is linked to
 - (C) a 3' non-translated sequence that functions in a plant cell to cause termination of transcription and addition of polyadenylated ribonucleotides to a 3' end of said mRNA molecule.
 12. A substantially purified nucleic acid molecule, wherein said nucleic acid molecule comprises a nucleic acid sequence having between 100% and 70% identity with a nucleic acid sequence of SEQ ID NO: 1 or a complement thereof.

No prior art is relied upon in support of the examiner's position.

GROUNDS OF REJECTION

Claims 3, 5-7, 9-10 and 12-20 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility.

Claims 12-19 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention.

We reverse the written description rejection, and remand the application to the examiner for further consideration of the utility and enablement rejections.

DISCUSSION

Written Description:

The examiner rejected the claims as inadequately described, on the basis that the claimed nucleic acids

comprise SEQ ID NO: 1 or a nucleic acid related to SEQ ID NO: 1 by a particular range of identity (i.e. 100% to 80% identity, as in claim 13)¹¹. This genus is sufficiently broad so as to encompass a multitude of variants of SEQ ID NO:1, as well as any full length coding sequence, mRNA, promoter, or genomic DNA of which SEQ ID NO: 1 is a portion, or of which the recited polynucleotides with identity to SEQ ID NO: 1 are portions. This large genus is represented in the specification by one species, a nucleic acid consisting of SEQ ID NO: 1.

Answer, bridging paragraph, pages 8-9 .

We will reverse this rejection. The written description requirement of 35 U.S.C. § 112, first paragraph, does not require a description of the complete structure of every species within a chemical genus. See Utter v. Hiraga, 845 F.2d 993, 998, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988) (“A specification may, within the meaning of 35 U.S.C. § 112, ¶ 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.”).

The Federal Circuit has held that “[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which

¹¹ While the examiner refers to claim 13, which depends from claim 12, we note as illustrated above, that claim 12 is broader than claim 13, in that it relates to a “sequence having between 100% and 70% Identity with a nucleic acid sequence of SEQ ID NO: 1 or a complement thereof.”

features constitute a substantial portion of the genus." University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Our appellate reviewing court has also held that the complete structure of a claimed DNA is not necessarily required. The court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'"

Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002) (emphasis omitted, alterations in original).

With respect to the claimed sequences that have 70% to 100% identity with SEQ ID NO:1, the Lilly court held that a genus could be described via "recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. The Enzo court held that such a description could take the form of "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." 296 F.3d at 1324, 63 USPQ2d at 1613. In this case, the complete structure of SEQ ID NO:1 has been described, and the nucleic acids of the claimed genus share 70 or more percent identity with the structure of SEQ ID NO:1. Thus, the structural features that are common to the genus make up 70% of the structure

of the claimed polypeptides. The examiner has not adequately explained why this degree of structural similarity is inadequate to "constitute a substantial portion of the genus," as required by Lilly.

Accordingly, we reverse the rejection of claims 12-19 under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention.

Utility:

The issues of whether a disclosure satisfies the "how to use" provision of 35 U.S.C. § 112, and the utility requirement of 35 U.S.C. § 101, are closely related. See In re Swartz, 232 F.3d 862, 863, 56 USPQ2d 1703 (Fed. Cir. 2000), Process Control Corp. v. HydReclaim Corp., 190 F.3d 1350, 1358, 52 USPQ2d 1029, 1034 (Fed. Cir. 1999), Newman v. Quigg, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989). Under the utility requirement, our appellate reviewing court, has held that it makes no sense to require claims to set forth inventions that satisfy all the disclosed objectives, but that "[w]hen a properly claimed invention meets at least one stated objective, utility under § 101 is clearly shown." Raytheon Co. v. Roper Corp., 724 F.2d 951, 958, 220 USPQ 592, 598 (Fed. Cir. 1983).

As set forth in In re Langer, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974), emphasis in original:

As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of Section 101 for the entire claimed subject matter unless there is reason for one skilled in the art to question

the objective truth of the statement of utility or its scope. Assuming that sufficient reason to question the statement of utility and its scope does exist, a rejection for lack of utility under Section 101 will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the statement of utility and its scope as found in the specification are true. Cf. In re Marzocchi, 58 CCPA 1069, 1073, 439 F.2d 220, 223, 169 USPQ 367, 369 (1971) (involving the enablement requirement of 35 U.S.C. 112, first paragraph).

According to the examiner (Answer, page 6), “[t]here has been no specific assertion that in fact SEQ ID NO: 1 is a promoter, aside from the claims.”

Contrary to the examiner’s assertion, however, appellant’s specification does set forth a statement of utility that corresponds in scope to the subject matter claimed. Specifically, appellant discloses (specification, page 16), “[a]nother class of agents of the present invention are nucleic acid molecules having promoter regions or partial promoter regions, including those located within SEQ ID NO: 1....” As set forth in Raytheon, “[w]hen a properly claimed invention meets at least one stated objective, utility under § 101 is clearly shown.”

Similarly, as set forth in Johns Hopkins Univ. v. CellPro Inc., 152 F.3d 1342, 1361, 47 USPQ2d 1705, 1714 (Fed. Cir. 1998), “[t]he enablement requirement is met if the description enables any mode of making and using the invention.”

Therefore, it is the examiner’s initial burden to establish that those skilled in this art would question the objective truth of the asserted utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (“Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence.”). In our opinion, the examiner has not provided sufficient evidence to

show that one of ordinary skill in the art would reasonably doubt that a nucleic acid molecule comprising SEQ ID NO: 1 would not have utility as a promoter as disclosed in appellants' specification.

To the contrary, the examiner has simply asserted (Answer, page 5) that "further experimentation would be required to reasonably confirm that SEQ ID NO: 1, or its complement, or fragments of either would function as a promoter as required by the claims. The specification does not provide any guidance as to the use of SEQ ID NO: 1, its complement or fragments thereof as promoters." Based on this assertion, the examiner concludes, "[t]he use of ... SEQ ID NO: 1 as a promoter is not a specific or substantial utility since further experimentation would be required to confirm that in fact SEQ ID NO: 1 has the ability to cause the production of an mRNA molecule...." Answer, page 6. While appellant has disclosed the characteristics of promoters within the scope of the claimed invention at pages 16-17 of the specification, the examiner fails to address this section of appellant's specification, or to establish a factual basis on this record to support the assertion that SEQ ID NO: 1 does not contain a promoter element.

According to the examiner (id.), "one would have to determine if the ... [promoter] is tissue specific or constitutive, for example, or if it is an inducible promoter, and under what circumstances it is induced or repressed in order to make use of the claimed plants." The examiner finds (id.), "[e]ach of these determinations is highly unpredictable, from the determination ... of the type of promoter it may be to the determination of fragments of the promoter that confer

promotion activity." The examiner, however, fails to establish a factual basis on this record to support these assertions.

Further, our review of this record is hindered by the examiner's failure to apply any type of claim construction to the claims now before us on appeal. In this regard, we note that claims 3 and 7, as well as the claims that depend from these claims, require in part "(A)" of each claim "an exogenous promoter region which functions ... to cause the production of a mRNA molecule." According to part "(A)" of these claims the promoter "comprises SEQ ID NO: 1 or a complement thereof...." We find no clear disclosure in the specification that SEQ ID NO: 1 is capable of functioning as a promoter region in plant cells to cause the production of a mRNA molecule. As we understand it, part "(A)" of these claims is open to at least three possible interpretations:

1. SEQ ID NO: 1 contains a promoter region which does function in plant cells to cause the production of a mRNA molecule,
2. SEQ ID NO: 1 does not contain a "promoter region," but instead contains a "regulatory element"² that acts in concert with a promoter region operably attached, either 5' or 3', to SEQ ID NO: 1, and thereby serves to regulate the expression of a mRNA molecule. For example, SEQ ID NO: 1 is an enhancer regions which is incapable of acts on a promoter, but is insufficient to function in plant cells to cause the production of a mRNA molecule on its own, or
3. SEQ ID NO: 1 contains neither a promoter region nor a regulatory element and simply serves as a filler sequence between the promoter region and a structural nucleic acid molecule, as defined in part "(B)" of these claims. For example, SEQ ID NO: 1 is incapable of functioning in plant cells to cause the production of a mRNA molecule, but instead serves only to

² See e.g. appellant's specification, page 17.

maintain the proper distance between a promoter and a "regulatory element."

It may be that the examiner is of the opinion that SEQ ID NO: 1 does not contain a promoter element. Cf. interpretation 3 above. The examiner, however, has not provided a sufficient evidentiary basis on this record to establish that SEQ ID NO: 1 does not contain a promoter or regulatory region, or if it does, why a person of ordinary skill in the art would reasonably doubt that the sequence would not function as a promoter or regulatory region.

For the foregoing reasons we remand the application to the examiner for further consideration. Prior to any further action on the merits, we encourage the examiner to take a step back and reconsider the claimed invention together with appellant's specification and the relevant prior art. In this regard, we remind the examiner as set forth in In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989), "claims must be interpreted as broadly as they reasonably, allow, in order to achieve complete exploration of applicant's invention and its relationship to prior art, so that ambiguities can be recognized, scope and breadth of language explored, and clarification imposed."

Accordingly, prior to taking any action on the record, we encourage the examiner to determine the broadest reasonable interpretation of the claimed invention and to include an analysis of this claim construction in any subsequent Office Action. If, after the examiner has evaluated the scope of the claim, the examiner believes that a rejection is necessary, the examiner should include on this record, an analysis of the claim construction together with a reasoned, fact-

based analysis of claimed invention together with the evidence necessary to support any such rejection.

In addition, we note that appellant has disclosed and argued that a nucleic acid molecule comprising SEQ ID NO: 1 has a number of utilities, e.g., for identifying the presence or absence of a polymorphism, or as probes for other molecules or as a source for primers (see e.g., Brief, pages 7-11). These issues and arguments, however, bear a close resemblance to those presented in Ex parte Fisher, 72 USPQ2d 1020 (Bd. Pat. App. & Int. 2004) (affirming the rejection of claim 1 under 35 U.S.C. § 101 and § 112, first paragraph.).

Accordingly, we encourage both the examiner and appellants to take the opportunity to reconsider their arguments on this record and to take into account the effect, if any, that Fisher may have on the issues under 35 U.S.C. § 101 and § 112, first paragraph.

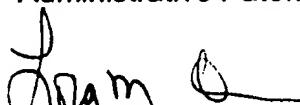
REVERSED-IN-PART and REMANDED


William F. Smith
Administrative Patent Judge

) BOARD OF PATENT


Donald E. Adams
Administrative Patent Judge

) APPEALS AND


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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 26

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JOSEPH R. BYRUM,
THOMAS J. La ROSA, and
GREGORY R. HECK,

Appeal No. 2002-0078
Application No. 09/206,040

ON BRIEF



Docketed
Due Date 10-20-03
Initial WB

Before STONER, Chief Administrative Patent Judge, and WILLIAM F. SMITH and SCHEINER, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from an examiner's final rejection of claims 1 through 3, which read as follows:¹

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¹ A copy of SEQ ID No. 1 is attached to this opinion.

1. A nucleic acid molecule isolated from other nucleic acid molecules and comprising SEQ ID No. 1 or its complement.
2. A nucleic acid molecule consisting of SEQ ID No. 1 or its complement.
3. A nucleic acid molecule isolated from other nucleic acid molecules and consisting essentially of SEQ ID No. 1 or its complement.

Claims 1 through 3 stand rejected under 35 U.S.C. § 101 (utility) and § 112, first paragraph (enablement). Claims 1 and 3 also stand rejected under 35 U.S.C. § 112, first paragraph (written description). We affirm the utility and enablement rejections and do not reach the merits of the written description rejection. Since our reasons for concluding that the claims lack patentable utility differ substantially from those advanced by the examiner, we denominate our affirmance as a new ground of rejection under 37 CFR § 1.196(b).

Background

The nucleic acid molecule set forth in SEQ ID No. 1 is stated to be an expressed sequence tag (EST) obtained from soybean plant material. Specification, page 14 ("The present invention provides soybean ESTs . . ."), Appeal Brief, page 2 ("The invention is directed to nucleic acid molecules reciting the sequence of an expressed sequence tag . . ."). ESTs are "short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1. As explained in Examples 1 and 2 of the specification, the claimed EST was obtained from a cDNA library prepared

from young soybean seeds collected from young pods.² The cDNA library from which the nucleic acid molecule set forth in SEQ ID No. 1 was isolated has been designated LIB3049. Specification, page 18.

The three claims before us for review define the claimed nucleic acid molecule as comprising, consisting of, or consisting essentially of SEQ ID No. 1 or its complement. Appellants explain that a nucleic acid molecule is said to be the 'complement' of another nucleic acid molecule if it exhibits complete complementarity, stating "[a]s used herein, molecules are said to exhibit 'complete complementarity' when every nucleotide of one of the molecules is complementary to a nucleotide of the other." Specification, page 16. However, appellants back away from this absolute definition of "complement" stating that "[d]epartures from complete complementarity are permissible, as long as such departures do not completely preclude the capacity of the molecules to form a double stranded structure." Specification, page 17.

The specification sets forth a number of utilities for the nucleic acid molecule of SEQ ID No. 1 which are summarized by the examiner as follows:

The utilities disclosed for the EST of SEQ ID NO: 1 or fragment thereof, or a nucleic acid molecule comprising same are:

² The record contains conflicting statements in regard to the source of the cDNA library from which the claimed EST was isolated. Example 1 states that the cDNA library was obtained from young seeds collected from young pods while page 24 of the specification states that the nucleic acid molecules of the present invention "were isolated from pods and seeds." (Emphasis added). Appellants summarize their invention at page 2 of the Appeal Brief stating that "[t]he claimed nucleic acid molecules were derived from a cDNA collection prepared from young soybean pods." Thus, it is unclear whether the cDNA library was obtained from young seeds, young pods, or a combination of young seeds and young pods. If prosecution is resumed on this subject matter, appellants should clarify the source of the claimed nucleic acid molecule.

sequences corresponding to the claimed nucleic acid molecule in a genome, and then use as a probe for detecting the polymorphisms, which serve as a molecular marker, either a) for a mutation affecting the expression of a product encoded, at least in part, by the claimed nucleic acid molecule (specification, pages 27-28) or b) for a desirable trait that is genetically linked to the polymorphism (specification, pages 35-36);

- Use of the EST as a probe for detecting a physical map location, e.g. as a marker in in situ hybridization;
- Use as a probe or source of PCR primers either to isolate other nucleic acid molecules (e.g. complete cDNA, protein coding sequence, genomic fragment, promoter, start of a chromosome walk) from the same organism or different organisms, i.e. other plants, or to detect other nucleic acid molecules (e.g. mRNA, chromosomal region, chromosome). Disclosed for the latter, for example, is to detect the mRNA in different tissues or as a measure of protein expression from the mRNA (based on mRNA levels), particularly if there is a mutation (hypothetical) affecting expression;
- Use of the EST as an antisense inhibitor of the corresponding mRNA; and
- Use as a probe to identify or isolate proteins that might bind to the EST sequence.

Examiner's Answer, pages 4-5. In the opinion of the examiner:

Each of these utilities requires additional knowledge about the EST before the EST can be used for a specific purpose, such as: whether there are sequence polymorphisms linked to the gene corresponding to the EST and, if so, their identity; the map location of the corresponding gene; the sequence of the corresponding complete mRNA sequence, protein coding sequence or genomic sequence; the function of the protein encoded by the corresponding mRNA; the identity and phenotype, if any, of a mutation in the corresponding gene; the tissue distribution of the corresponding mRNA and tissue-specific expression levels; etc. The specification does not provide any such information specific to the disclosed EST. Consequently, the disclosed utilities are non-specific utilities, since any of the general disclosed utilities would apply equally to any uncharacterized nucleic acid molecule from soybean in particular, or plants in general.

Examiner's Answer, paragraph bridging pages 5-6.

The examiner concludes:

In Brenner v. Manson, 148 USPQ 689, 696 (US, 1966), the Court held that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." The original disclosure lacks any successful conclusion for even one of the vague and general utilities disclosed. Thus, no "substantial" or "real world" utility has been disclosed.

Examiner's Answer, page 6.

Appellants urge that the claims on appeal possess patentable utility under 35 U.S.C. § 101. See, e.g., Appeal Brief, page 19 ("Applicants have disclosed numerous utilities for the claimed nucleic acid molecules, and have submitted evidence proving that the claimed nucleic acid molecules work for at least two of the disclosed utilities."). In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. Appeal Brief, pages 11-18.

In support of their position, appellants rely upon the declaration of Dr. Roger C. Wiegand.³ Dr. Wiegand states that "EST databases are useful tools that may be used to select clones for further research, or to compare sequences in the database with other sequences, but the nucleic acid molecules represented by the ESTs themselves have value beyond that associated with their ESTs." Wiegand decl., para. 6. Dr. Wiegand also states that "ESTs are typically used to develop molecular markers,

³ Appellants also refer to a La Rosa declaration in the heading appearing on page 4 of the Appeal Brief. However, the La Rosa declaration is only directed to the deposit of clone designated LIB-3049-003-Q1-E1-H7 with the ATCC.

Examiner's Answer, page 7. The examiner has determined that claims 1 and 3 embrace an "essentially infinite genus of nucleic acid molecules" (Examiner's Answer, page 8) and that the specification does not "teach the maximum length or locations (5' end, 3' end, or both ends, of nucleic acid sequence(s) that could be added to SEQ ID NO: 1, that would not interfere with its disclosed use as a hybridization probe." Id... The examiner is also of the opinion that "[s]ince the claims embrace adding any and all nucleic acid sequences to the core nucleic acid molecule SEQ ID NO: 1, one cannot predict whether or not the additional nucleic acid sequence[s] added would hybridize to a target nucleic acid molecule other than the intended target nucleic acid molecule. When such a situation occurs, and more than one nucleic acid molecule is amplified or detected in hybridization, the skilled artisan would have no information that would allow the desired target nucleic acid molecule to be distinguished from a nucleic acid molecule that was targeted by the added nucleic acid sequences." Examiner's Answer, page 9. The examiner concludes:

Consequently, making the myriad of nucleic acid molecules embraced by the claims and testing the suitability of each for use as a probe or primer for the disclosed utilities in the absence of guidance or examples would require excessive trial and error experimentation due to the unpredictability involved, and would therefore require undue experimentation.

Id.

In reaching the conclusion of undue experimentation, the examiner did not perform an analysis of the so-called Wands factors. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988). In contrast to the examiner's position,

hybridization probes, amplification primers, and to identify the presence or absence of polymorphisms." Wiegand decl., para. 7. Dr. Wiegand also discusses the results of tests performed with a nucleic acid molecule "having the sequence of SEQ ID No. 1" in regard to its use as a hybridization probe in detection of genetic polymorphism, stating:

19. The results of the northern blots indicate that a nucleic acid molecule having the sequence of SEQ ID NO: 1 can be synthesized and successfully used as a hybridization probe, and that such a molecule will hybridize to a naturally occurring soybean nucleic acid molecule. Accordingly, a nucleic acid molecule having SEQ ID NO: 1 is useful as a hybridization probe for expression profiling or other purposes.

21. I believe that a nucleic acid molecule comprising the EST of SEQ ID NO: 1 possesses the practical utility of being useful for detecting polymorphisms because scientists under my supervision performed Southern blots to test if a synthetic nucleic acid molecule based on SEQ ID NO: 1 would detect polymorphisms. It did.

23. The results of the Southern blots indicate that a nucleic acid molecule having the sequence of SEQ ID NO: 1 can be synthesized and successfully used to detect polymorphisms in soybean chromosomal DNA. Accordingly, a nucleic acid molecule having the sequence of SEQ ID NO: 1 is useful for detecting polymorphisms in order to develop a genetic map, determining if a plant carries the gene for a particular trait, determining the copy number of a particular gene in a plant, or for other purposes.

Wiegand decl., paras. 19, 21, and 23.

In regard to claim construction, the examiner states in the context of setting forth the enablement rejection:

The recitation of "consisting essentially of" in claim 3 has been treated as being equivalent to "comprising", as recited in claim 1. There is nothing on the record to indicate how "consisting essentially of" alters the scope of claim 3 compared to claim 1. Thus, claim 3 would not exclude any embodiment embraced by claim 1.

appellants provide an analysis of the Wands factors in support of their position that the claim are enabled. Appeal Brief, pages 27-36.

The examiner's reasoning in regard to the written description rejection is:

Claims 1 and 3 are drawn to nucleic acid molecules "comprising" or "consisting essentially of" the EST of SEQ ID NO: 1; and therefore to an astronomically large genus of nucleic acid molecules comprising SEQ ID NO: 1 even solely considering nucleic acid sequences and ignoring nucleic acid molecules comprising non-nucleotide moieties such as detectable labels. The specification does not explicitly disclose any nucleic acid molecules that "comprise" or "consist essentially of" SEQ ID NO: 1, other than that of SEQ ID NO: 1 itself (either unlabeled or labeled with a detectable non-nucleotide moiety such as a fluorophor) and the clone from which the sequence was derived. Any additional cDNA sequence that may be present on the clone was not described other than by deposit. No nucleic acid molecules are disclosed wherein the nucleic acid sequence is extended beyond SEQ ID NO: 1, other than solely by implication a larger EST or mRNA comprising SEQ ID NO: 1. However, the specification does not disclose the structure of any such larger nucleic acid molecule or EST or mRNA. The disclosure of the single nucleic acid molecule set forth as SEQ ID NO: 1 does not adequately describe the astronomically large number of possible nucleic acid molecules embraced by claims 1 and 3.

Examiner's Answer, page 10.

Appellants respond that the specification reflects their "possession" of the claimed invention. Appeal Brief, pages 36-41.

Discussion

As always, we begin our analysis by construing the claims as "the name of the game is the claim." In re Hiniker Co., 150 F.3d 1362, 1369, 47 USPQ2d 1523, 1529 (Fed. Cir. 1998)(citing Giles Sutherland Rich, Extent of Protection and Interpretation of Claims--American Perspectives, 21 Int'l Rev. Indus. Prop. & Copyright L. 497, 499 (1990). See also, Panduit Corp. v. Dennison Manufacturing Co., 810 F.2d 1561, 1567-

68, 1 USPQ2d 1593, 1597 (Fed. Cir.), cert. denied, 481 U.S. 1052 (1987) ("Analysis begins with a key legal question--what is the invention claimed? ... Claim interpretation ... will normally control the remainder of the decisional process."). The claim analysis which appears in the Appeal Brief and the Examiner's Answer provides little assistance in our review of the issues presented in this appeal. For example, appellants state "[t]he genus of claimed nucleic acid molecules, i.e., nucleic acid molecules 'comprising,' 'consisting of,' and 'consisting essentially of' SEQ ID No. 1 have been described by the recitation of a 'basic and novel' common structural feature - the nucleotide sequence of SEQ ID No. 1 - which distinguishes them from nucleic acid molecules not in the claimed genus." Appeal Brief, page 4. Appellants have not explained on this record how a nucleic acid molecule which "comprises" the nucleotide sequence of SEQ ID No. 1 differs from a nucleic acid molecule "consisting of" or "consisting essentially of" the nucleotide sequence of SEQ ID No. 1. Appellants' arguments for the most part are couched in vague, non-specific terms such as "the claimed nucleic acid molecules," instead of referring to actual claims and the language used therein. See, e.g., Appeal Brief, page 8, first full paragraph ("Applicants have asserted specific utilities for the claimed nucleic acid molecules...."). Importantly, appellants have not offered any assistance in the Appeal Brief as to how broadly or narrowly they would have the word "complement" construed as it is used in claims 1-3 on appeal.

The one specific statement we find in the Examiner's Answer construing the claims on appeal is contrary to governing precedent and, thus, is in error. The examiner states "[t]he recitation of 'consisting essentially of' in claim 3 has been treated

as being equivalent to 'comprising', as recited in claim 1. There is nothing on the record to indicate how 'consisting essentially of' alters the scope of claim 3 compared to claim 1. Thus, claim 3 would not exclude any embodiment embraced by claim 1."

Examiner's Answer, page 7, fourth full paragraph. The examiner's holding that the transitional phrase "consisting essentially of" is equivalent to the transitional phrase "comprising" is contrary to long established precedent. In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 896 (CCPA 1963) ("The word 'essentially' opens the claims to the inclusion of ingredients which would not materially affect the basic and novel characteristics of appellants' compositions as defined in the balance of the claim, according to the applicable law."). Assuming the examiner is correct in concluding there is "nothing on the record" that would allow the examiner to distinguish between a claim using the transitional phrase "consisting essentially of" and the same claim using the transitional phrase "comprising," we do not find that to be sufficient justification for the examiner to upend decades of precedent. These transitional phrases have defined meanings in the law. The fact that an examiner is having trouble distinguishing the scope of claims 1 and 3 on the basis of the transitional phrases used may, however, be an indication that the claims are indefinite under 35 U.S.C. § 112, second paragraph. In re Hammack, 427 F.2d 1378, 1382, 166 USPQ 204, 208 (CCPA 1970) (Purpose of 35 U.S.C. § 112, second paragraph, "is to provide those who would endeavor, in future enterprise, to approach the area circumscribed by the claims of a patent, with the adequate notice demanded by due process of law, so that they may more readily and

accurately determine the boundaries of protection involved and evaluate the possibility of infringement and dominance.").

Additional ambiguity is injected in the claims by use of the word "complement" and the reference in the claims to SEQ ID No. 1. As discussed above, the specification contains a very strict definition of complement, i.e., every nucleotide of one of the molecules is complementary to a nucleotide of another nucleic acid molecule, while at the same time indicating that the nucleic acid molecules according to the present invention may depart from "complete complementarity." Thus, determining what constitutes a "complement" of the claimed nucleic acid molecules as that word is used in the claims on appeal is problematic.

The reference in the claims to SEQ ID No. 1 is also subject to interpretation as appellants state "[a]n aspect to the present invention is that the nucleic acid molecules of the present invention include nucleic acid molecules that are degenerate of that set forth in SEQ ID No. 1." Specification, page 18. As acknowledged by appellants, "a nucleic acid molecule is degenerate of another nucleic acid molecule when the nucleic acid molecules encode for the same amino acid sequences but comprise different nucleotide sequences." Id. The nucleotide sequence depicted in SEQ ID No. 1 does not indicate the reading frame or contain an assigned amino acid sequence. Without such knowledge, it is unclear how one would consider a given nucleotide sequence to be "degenerate" of that depicted in SEQ ID No. 1. Thus, if the claims on appeal are to be read as encompassing degenerate nucleotide sequences, the determination of the identity of such degenerate molecules would be difficult.

Having a firm understanding of the scope of the claims under review is also necessary in evaluating appellants' rebuttal evidence in regard to the utility rejection. For example, Dr. Wiegand states "the synthetic probe is a true enough copy of SEQ ID No. 1 for use as a probe to demonstrate the utility of nucleic acid molecules characterized by SEQ ID No. 1." Wiegand Declaration, para. 16. (Emphasis added). If one cannot readily determine whether a given nucleotide sequence is within or without the scope of the claims under review, it is difficult to assign weight to evidence which is based upon "a true enough copy of SEQ ID No. 1."

The ability or inability to reasonably ascertain the metes and bounds of a claim is important in determining whether the claim possesses patentable utility under § 101 as all embodiments within a claim must meet the utility requirement. In re Langer, 503 F.2d 1380, 1394, 183 USPQ 288, 299 (CCPA 1974) ("We hold that appellant's evidence of record is insufficient to rebut the prima facie case for lack of utility in the subject matter (other than [preferred species]) recited in these claims."). In similar fashion, it is difficult to determine whether a given claim is enabled throughout its scope without undue experimentation without first knowing the scope of the claim under review. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 238 (CCPA 1971) ("Once having determined that the subject matter defined by the claims is particular and definite, the analysis then turns to the first paragraph of § 112 to determine whether the scope of protection sought is supported and justified by the specification disclosure.") (Emphasis added). The same holds true in considering the written description requirement of the first paragraph of § 112. Enzo Biochem, Inc. v. Gen-Probe, Inc., 296

F.3d 1316, 1327, 63 USPQ2d 1609, 1615 (Fed. Cir. 2002) ("On remand, the court should determine whether a person of skill in the art would glean from the written description, including information obtainable from the deposits of the claimed sequences, subsequences, mutated variants and mixtures sufficient to demonstrate possession of generic scope of the claims.").

Reaching a decision on a record such as this is difficult. However, we do know that the claims on appeal include one discrete and definite embodiment not subject to interpretation, alternative construction, ambiguity or spin of any type, i.e., the precise 469 nucleotide sequence set forth in SEQ ID No. 1 without any preceding or trailing nucleotides.

Thus, we will proceed to a decision on the issues raised in this appeal to the extent that claims 1 through 3 on appeal include the nucleic acid molecule defined by the 469 nucleotide sequence set forth in SEQ ID No. 1 without alteration or any preceding or trailing nucleotides as this is the only subject matter that we can say with certainty is included within each of the claims.

1. Utility.⁴

The starting point for determining whether a nucleic acid molecule having the 469 nucleotide sequence set forth in SEQ ID No. 1 possesses utility under 35 U.S.C.

⁴ Appellants refer to the "Revised Utility Examination Guidelines, 64 Fed. Reg. 71440, 71442" in presenting their case on appeal. See, e.g., Appeal Brief, page 5. Those guidelines were superseded by Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001). Although the Appeal Brief and the Examiner's Answer were prepared after that date, it does not appear that either appellants or the examiner considered the latest version of the guidelines in preparing the briefing in this appeal. Be that as it may, we note that the utility guidelines expressly state that they do not have the force or effect of law, see id. at 1098, and our analysis is based instead on controlling precedent. We note, however, that our conclusion is consistent with the utility guidelines.

§ 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). The Court stated "the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.⁵ In considering the issues presented in this appeal, special attention must be paid to the Court's statement that a patent should issue only when an invention possesses "substantial utility," *i.e.*, "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that

⁵ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, has used the phrases "substantial utility" and "practical utility" interchangeably. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1963-1964, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

"where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁶

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

⁶ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d

936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroid research and in the application of steroid materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. See id., 26 USPQ2d at 1606. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id., 26 USPQ2d at 1605.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one

was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds . . . , analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be

met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, *i.e.*, identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 28-35 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification is not specific to the 469 nucleotide molecule depicted in SEQ ID No. 1. Nor does the specification explain why the 469 nucleotide molecule of SEQ ID No. 1 would in fact be useful in detecting polymorphisms. Rather, appellants' argument is that "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." Appeal Brief, page 14. In other words, appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage and can be viewed to be at the lower end of the utility spectrum. At the high end of the utility spectrum would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge of the gene and its role in the plant's development and phenotype (the present circumstances) and having

complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

Dr. Wiegand's declaration does not aid appellants in this aspect of their case. Polymorphism as a utility is discussed primarily in paragraphs 20-23 of the declaration. Two probes were used in Dr. Wiegand's work, "a synthesized nucleic acid molecule based on overlapping oligomers matching SEQ ID No. 1; and a probe derived from the plasmid that carries clone LIB3049-003-Q1-E1-H7, from which SEQ ID No. 1 was determined." Dr. Wiegand concludes that "a nucleic acid molecule having a sequence of SEQ ID No. 1 can be synthesized and successfully used to detect polymorphisms in soybean chromosomal DNA. Accordingly, a nucleic acid molecule having the sequence of SEQ ID NO. 1 is useful for detecting polymorphisms in order to develop a genetic map, determining if a plant carries the gene for a particular trait, determining the copy number of a particular gene in a plant, or for other purposes."

First, the precise identity of the nucleic acid molecules used in Dr. Wiegand's work is unclear. As stated above, we are limiting our consideration of the issues raised in this appeal as they pertain to the precise 469 nucleotide molecule set forth in SEQ ID No. 1. Dr. Wiegand's conclusions are premised upon use of "a nucleic acid molecule having the sequence of SEQ ID No. 1." It is unclear whether the probes used contained only the specific 469 nucleotides depicted in SEQ ID No. 1 or contained

additional nucleotides before and/or after the specific 469 nucleotide molecule set forth in SEQ ID No. 1.

In any case, it is not clear how the results reported in the declaration establish a substantial utility. Dr. Wiegand does not state in his declaration that these results provide any significant knowledge. To the contrary, they appear to represent what one might reasonably assume--a given EST may or may not detect a polymorphism in a related organism. While such knowledge may indicate the molecule is "useful" to some degree, we do not find that it represents a substantial utility.⁷

b. Probes or source of primers

Appellants argue that the specification "discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Appeal Brief, page 16. While that may be true, it begs the question of what substantial use such knowledge would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to the 469

⁷ We are aware that the examiner and appellants have engaged in a discussion on this record as to whether the specific soybean plants used in Dr. Wiegand's work are species and thus, whether the work is relevant in determining the utility issue. However, the manner in which the examiner and appellants have raised this issue in the context of this appeal proceeding does not provide a reasonable basis for its review. As stated by appellants, the issue was raised in an Advisory Action. Appeal Brief, page 15. Appellants responded to the assertions made in the Advisory Action by relying upon a dictionary definition in the Appeal Brief. The examiner discusses this portion of the Appeal Brief on pages 34-35 of the Examiner's Answer, stating that the cited dictionary reference was not provided and could not be evaluated by the examiner. The examiner then goes on to cite two other documents in support of his position. Appellants did not file a Reply Brief.

An appeal should be contested upon a fixed record, not upon an ever expanding and shifting record as here. It does not appear that appellants made the requisite showing under 37 CFR § 1.195 in presenting new evidence in conjunction with this appeal nor is it apparent that the examiner had authority to rely upon new evidence in support of his position. Under these circumstances, we decline to consider the issue.

nucleotide molecule of SEQ ID No. 1. Why does knowledge that a similar molecule may exist in another organism represent a substantial utility?

The same analysis holds for the stated utility that a nucleic acid molecule may be used in a "chromosome walk." Id., pages 16-17. In presenting this argument, appellants run afoul of the confusion engendered as to the source of the present nucleic acid molecules. Appellants' argument at page 17 of the Appeal Brief is couched in terms of the ability to isolate a promoter that is active in young seed pods (5 to 15 days after flowering). It appears that this argument is premised upon the fact that the nucleic acid molecule of the present invention was obtained from young seed pods. However, as explained above, the examples of the specification state that the nucleic acid molecule was obtained from young seeds collected from young pods.

Appellants state that the examiner denigrated the "chromosome walk" utility by stating in the Final Rejection that "[a]ny nucleic acid molecule from any plant cell generally serves this purpose...." Appeal Brief, page 16. Appellants argue in essence that despite the fact that the argued utility applies to all ESTs, there is no legal requirement that an invention's utility be "unique" to the invention, i.e., an invention can be a member of a class, where all the members of the class share a common utility.

First, appellants have only been required to identify a utility that is specific to the invention claimed. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form.). An invention certainly can have a utility that is shared by other compounds or compositions. Take, for

example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

Nor does Dr. Wiegand's declaration assist appellants in this portion of their position on appeal. Dr. Wiegand discusses the use of EST's to generate probes in paragraphs 14-17 of his declaration. However, that work is based upon a synthetic probe stated to be "a true enough copy of SEQ ID No. 1." It is not apparent why evidence based upon "a true enough copy" of SEQ ID No. 1 is relevant in this appeal.

c. Other Arguments⁸

Appellants argue that the specification describes other utilities for the claimed nucleic acid molecules including "introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Appeal Brief, page 10. Specifically, appellants argue that a compound can be provided to both an antisense plant and a control plant not having antisense, with the effect of the compound on the plant being monitored. Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (page 64) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the co-suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized as here. Such a use does not provide a specific or substantial benefit in currently available form.

⁸ Appellants present arguments in the Appeal Brief responding to issues apparently raised by the examiner previously but not maintained in the statement of rejection in the Examiner's Answer. For example, appellants argue that the examiner was incorrect as characterizing the claimed nucleic acid molecules as "tools" in the Final Office Action and Advisory Action. Appeal Brief, pages 11-12. However, the examiner does not characterize the claimed nucleic acid molecules in that manner in stating the utility rejection on pages 4-7 of the Examiner's Answer. Appellants also present arguments on pages 23-26 of the Appeal Brief in regard to whether the claimed nucleic acid molecules correspond to a pseudogene or are an artifact. However, in presenting his position on appeal the examiner does not rely upon either theory in stating the rejection, Examiners Answer, pages 4-7. Apparently, the examiner no longer relies upon these rationales. Thus, we need not consider these issues.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular markers. Appeal Brief, pages 10-11. In regard to microarrays, appellants argue that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. Reference to para. 14 of the Wiegand declaration is made in support. Appeal Brief, page 11, n. 5. Dr Wiegand states "Soybean DNA clones are routinely used to detect expression levels of corresponding naturally occurring soybean nucleic acids. A nucleic acid molecule of SEQ ID NO: 1 can also certainly be used to detect expression level. Use of a nucleic acid molecule representing an EST as an expression probe is a practical use because it enables the detection of changes in expression of a particular gene." Wiegand decl., para. 14.

We find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in SEQ ID NO: 1. However, the specification provides no guidance which would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the SEQ ID NO: 1-specific information derived from a gene expression experiment would mean.

Suppose, for example, that a researcher found that SEQ ID NO: 1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO: 1 expression would depend on other factors, but again the specification provides no hint what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using SEQ ID NO: 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the

specification does not disclose how to use SEQ ID NO: 1-specific gene expression data.

Here, appellants assert that SEQ ID NO: 1, along with every other expressed soybean gene or protein, or for that matter, any expressed gene or protein, can be used to monitor changes in gene expression. However, without additional information, any observed results of changed expression of SEQ ID NO: 1 would have no meaning. The specification in effect discloses that the claimed nucleic acids can be used to monitor gene expression, and those of skill in the art will figure out what to do with the gene expression data. This utility is not substantial; it does not provide a specific benefit in currently available form.

Assuming arguendo that a generic gene expression assay—one based on monitoring expression of thousands of uncharacterized nucleic acids would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture.

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently

available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants assertion that the nucleic acid depicted in SEQ ID NO: 1 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of SEQ ID NO: 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the “growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs.” Appeal Brief, pages 19-21. Reliance is placed on paragraph 6 of the Wiegand declaration in support of this argument. Dr. Wiegand statements in this paragraph of his declaration refer to EST databases, clone sets and microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the

uncharacterized nucleic acid of SEQ ID NO: 1 in such devices represents a substantial use.

2. Enablement

There are two rationales set forth in the Examiner's Answer for this rejection. First, claims 1-3 are considered to be non-enabled "since the claimed invention is not supported by either a specific asserted utility or a well established utility for the set forth [in support of the § 101 rejection]. one skilled in the art clearly would not know how to use the claimed invention." Examiner's Answer, page 7. The examiner's second position focuses on claims 1 and 3 and their use of the transitional phrases "comprising" and "consisting essentially."

In regard to the first rationale, it appears that the rejection is simply a corollary of the finding of lack of utility. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue.⁹ On this basis we affirm the enablement rejection.

3. Written description

Only claims 1 and 3 are rejected under this section of the statute. The examiner has concluded that the use of the transitional phrases "comprising" and "consisting essentially of" in these claims results in appellants claiming an "astronomically large

⁹ Under these circumstances we need not reach the examiner's second rationale. However, we point out that the second rationale is premised upon an erroneous claim construction, i.e., the transitional phrases "comprising" and "consisting essentially of" are equivalent. If prosecution is resumed on this subject matter, the examiner should revisit the issue and construe "comprising" and "consisting essentially of" consistent with their well defined meanings. Also, as noted previously, the examiner did not make of record a fact-based analysis of the Wands factors. We urge the examiner in making any future enablement rejection, the rejection include an explicit analysis of the Wands factors.

genus of nucleic acid molecules" which are not "adequately describe[d]" by SEQ ID NO:

1. Examiner's Answer, page 10.

We do not find that this issue is ripe for review at this time and therefore decline to reach the merits of this rejection. The Appeal Brief was filed on January 31, 2001 and the Examiner's Answer was entered on August 6, 2001. Prior to the briefing in this appeal, the USPTO issued "Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) (Guidelines). Neither appellants nor the examiner discussed the Guidelines and determined what affect, if any, they may have on their respective positions. In addition, the Federal Circuit has recently considered written description issues involving claims directed to nucleotide sequences and their use in hybridization assays in Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002).

We believe a reasoned review of this rejection can only be performed after appellants and the examiner have had an opportunity to review the Guidelines and the court's opinion in Enzo. Since our affirmance of the utility rejection and the enablement rejection to the extent it is a corollary of the utility rejection constitutes a disposition of the appeal, we see no reason to remand the case for consideration of this issue now. Rather, if prosecution is resumed in this case, appellants and the examiner should revisit the issue and take into account the Guidelines and the guidance provided in Enzo.

Time Period For Response

This opinion contains a new ground of rejection pursuant to 37 CFR § 1.196(b). 37 CFR § 1.196(b) provides that, "A new ground of rejection shall not be considered final for purposes of judicial review."

37 CFR § 1.196(b) also provides that appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (§ 1.197(c)) as to the rejected claims:

(1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner. . . .

(2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED; 196(b)

Bruce H. Stoner, Jr.
Bruce H. Stoner, Jr., Chief
Administrative Patent Judge
)

William F. Smith
William F. Smith
Administrative Patent Judge
)

Toni R. Scheiner
Toni R. Scheiner
Administrative Patent Judge
)

) BOARD OF PATENT
)

) APPEALS AND
)

) INTERFERENCES

Appeal No. 2002-0078
Application No. 09/206,040

Page 35

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APPENDIX

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gctgcgaaag acgacagaag ggggggggaa agagagtgg a ttettggtga ctttcttgc 120
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gaaggctgtg gcaggacgca gagaatcgag ttatctcat caaagagctc gataggatca 420
ctggccaggc acatctgct atatctgtgg atgatacatt gaagatnnt 469

The opinion support of the decision being entered today is not written for publication and is not binding precedent of the Board.

Paper No. 17



UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DANE K. FISHER, and RAGHUNATH V. LALGUDI

Appeal No. 2002-2046
Application No. 09/619,643

HEARD: March 16, 2004

MAILED

MAR 31 2004

U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

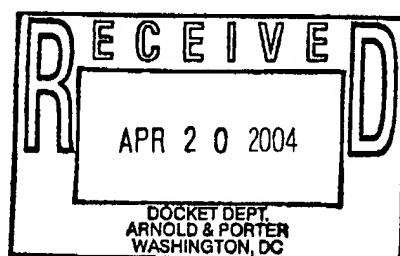
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 1, the only claim pending in the application, reproduced below:

1. A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5.

The examiner does not rely on a reference.



GROUNDS OF REJECTION

Claim 1 stands rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. Claim 1 also stands rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention. We affirm the utility and enablement rejections. We reverse the written description rejection.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags (ESTs). See Specification, page 15, lines 9-10. ESTs "are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1.

As set forth at page 9, lines 2-4, of appellants' specification "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 32236." Of these 32,236 nucleic acid sequences, the originally filed claims were directed to SEQ ID NO: 1 through SEQ ID NO: 4,013. On January 26, 2001 (Paper No. 4), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants "to elect up to 5 nucleic acid sequences" for consideration on the merits. Paper No. 4, page 3. In response, appellants elected SEQ ID NO:1 through SEQ ID NO:5. The ESTs set forth in SEQ ID NO: 1 through SEQ ID NO:

5 are disclosed to be obtained from cDNA library LIB3115 "generated from maize (RX601, Asgrow Seed Company, Des Moines, Iowa U.S.A.) pooled leaf tissue...." Specification, pages 79-80, Example 1.

The specification sets forth a number of utilities for the nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 which are summarized by the examiner (Answer, bridging paragraph, pages 5-6) as follows:

The specification teaches that the nucleic acids may be used to produce a plant containing reduced levels of a protein (pg. 11), determining an association between a polymorphism and a plant trait (pg. 11), isolating a genetic region or nucleic acid (pg. 11), determining a level or pattern in a plant cell of a protein in a plant (pg. 11), determining a mutation in a plant whose presence is predictive of a mutation affecting a level or pattern of a protein (pg. 13), as molecular tags to isolate genetic regions, isolate genes, map genes, and determine gene function (pg. 14), and identifying tissues (pg. 14).¹ The specification states that the nucleic acid ESTs of the present invention can enable the acquisition of molecular markers, which can be used in breeding schemes, genetic and molecular mapping and cloning of agronomically significant genes (pg. 31).

In the examiner's opinion "[t]hese are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acids being claimed." Answer, page 6. For example, the examiner finds (Answer, page 10), "determining whether the claimed nucleic acids have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way."¹

¹ During the Oral Hearing, appellants' representative confirmed that the administrative file contained no evidence that the claimed ESTs were capable of detecting a polymorphism that correlated with any particular trait.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See e.g., Brief, pages 6-12. According to appellants (Brief, page 3), "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of maize plants." Furthermore, appellants assert (Brief, page 8), "[t]he specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...."

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5. According to appellants' specification (page 15, lines 19-25), the term "substantially purified"

refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the claimed invention the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of

the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5.² In this regard, we recognize, as does the examiner (Answer, page 14), the claim as written encompasses, *inter alia*, genes, full open reading frames, fusion constructs, and cDNAs.

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, selected from the group consisting of the nucleic acid molecule defined by the 429 nucleotide sequence set forth in SEQ ID NO: 1, the 413 nucleotide sequence set forth in SEQ ID NO: 2, the 365 nucleotide sequence set forth in SEQ ID NO: 3, the 414 nucleotide sequence set forth in SEQ ID NO: 4, and the 333 nucleotide sequence set forth in SEQ ID NO: 5, with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5

² This interpretation of the claimed invention was confirmed by appellants' representative during the Oral Hearing.

possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695³,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," *i.e.*, "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a

³ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1963-1964, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁴

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

⁴ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of

§ 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroid research and in the application of steroid materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the

researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in

cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar

compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use

as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 35-42 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5. To the contrary, according to appellants' specification (page 35, lines 25-26), "one or more of the [32,236] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify ... polymorphism(s)." The specification does not explain why any of the 32,236 nucleotide molecules disclosed in the specification, or more specifically the five nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, would in fact be useful in detecting polymorphisms.

Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, bridging paragraph, pages 10-11):

Polymorphisms are natural variations within sequences which themselves may not have any meaningful use. Therefore, determining whether the claimed nucleic acids [(or nucleic acids detected by the claimed nucleic acids)] have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way. The [a]ppellant also argues, "many of these uses are directly analogous to a microscope". This argument has been reviewed but is not convincing because the microscope provides information to the scientist which is automatically useful. For example, the microscope may be used for identification and differentiation between gram-positive and gram-negative bacteria. The differentiation of bacteria facilitates in the administration of proper antibiotics. For example, if the microscope is used to determine whether Staph is present or whether Strep is present provides valuable information to the scientist and/or doctor for treating patients. The instant invention, however, provides no information to this extent. If the scientist determines that SEQ ID NO: 1 is present, the scientist does not know how to use this information. Thus, the identification of SEQ ID NO: 1 is not a substantial utility.

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further

define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Appeal Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to any of the nucleotide molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In the absence of such information, using the claimed molecules to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Brief, pages 8-9. According to appellants (Brief, page 9),

The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in leaves at the time of anthesis. Isolation of such a promoter would be desirable and particularly useful because it allows expression of proteins at that important developmental state, including proteins that provide disease resistance. Because the claimed nucleic acid molecules were isolated from leaves, they provide an appropriate starting point for isolating a promoter active in leaves. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter.

As we understand this argument, the claimed ESTs may be useful in searching for promoters that are only active in leaves at the time of anthesis. The

specification, however, fails to demonstrate that any of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5 would be useful in obtaining a successful result from such a search. As set forth at page 34, lines 14-19 of appellants' specification,

The [32,236] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced[,] tissue specific, cell-specific, cell -type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 32,236 nucleic acid molecules disclosed in the specification, or more specifically the five nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles.

Furthermore, notwithstanding appellants' assertion (Brief, page 9), there is no evidence on this record that any of the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are tissue or cell-type specific, or developmentally or environmentally regulated. In this regard, we note that the claimed nucleic acid molecules were isolated from the cDNA library LIB3115. Specification, page 80, lines 5-6. There is no evidence on this record that LIB3115 is a subtractive cDNA library, wherein nucleic acid molecules from other maize tissue, or from other developmental stages, was subtracted (removed)

from the library. Compare, for example, the subtractive cDNA library LIB3153 which is disclosed (specification, page 83, lines 17-19) to be "generated by subtracting driver cDNA, which is prepared from kernels harvested from 15 DAP [days after pollination] maize plants, from target cDNA, which is prepared from endosperms harvested from 5-8 day[s] after pollination (DAP) maize plants." In contrast to the claimed nucleic acid molecules, nucleic acid molecules SEQ ID NO: 24,931 through SEQ ID NO: 25,680 are from the subtractive cDNA library LIB3153.

In our opinion, the claimed nucleic acid molecules having the sequences identified as SEQ ID NO: 1 through SEQ ID NO: 5, represent five randomly selected nucleic acid molecules isolated from pooled leaf tissue at the time of anthesis. Notwithstanding appellants' emphasis on "anthesis," for the foregoing reasons, we find no evidence on this record that any of appellants' five randomly selected nucleic acid molecules are expressed only at the time of "anthesis." Accordingly, despite appellants' assertion to the contrary, there is no reasonable expectation that any of the claimed nucleic acid molecules would be capable of isolating a promoter that was only active in leaves at the time of anthesis. As appellants recognize (Brief, page 9), "[a] random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter" compared to a nucleic acid molecule that is known to be specifically associated with this stage of plant development.

We recognize appellants' argument (Brief, bridging sentence, pages 9-10), "[a]n invention may be 'less effective than existing devices but nevertheless

meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986)." While we agree with appellants' statement, we fail to see how it applies to appellants' claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Brief, page 6. Specifically, appellants argue (*id.*) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." *Id.*

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (page 73, line 17 through page 74, line 17) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized⁵ as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology

⁵ To emphasize the uncharacterized nature of appellants' invention we note the examiner's finding (Answer, page 17) that translating SEQ ID NO: 5 in all 6 possible reading frames reveals that the sequence contains numerous stop codons which would terminate the translation of a protein, or protein fragment, encoded thereby.

and use as molecular markers. Brief, page 6. In regard to microarrays, appellants argue (*id.* fn. 3) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in e.g., SEQ ID NO: 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the SEQ ID NO: 1-specific information derived from a gene expression experiment would mean. As the examiner points out (Answer, page 9), "the instant claimed nucleic acids appear to require further experimentation on the material itself to determine the function and properties of the claimed nucleic acids."

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO: 1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO: 1 expression would depend on other factors, but again the specification provides no hint as to what other factors

might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using SEQ ID NO: 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1-specific gene expression data.

Assuming arguendo, that a generic gene expression assay—one based on monitoring expression of thousands of uncharacterized nucleic acids would provide a useful tool for, e.g., drug discovery, it does not follow that each one of

the nucleic acids represented in the assay individually has patentable utility.

Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form.

Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard.

The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are

useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of SEQ ID NO: 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 in such devices represents a substantial use.

For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101.

Enablement

According to the examiner (Answer, page 13, emphasis removed), "since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth [in support of the rejection under 35 U.S.C. § 101] one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), this rejection should be reversed for the same reasons set forth in their arguments regarding the

rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

Written description

This rejection stands on a different footing. As we understand the examiner's argument the use of the transitional phrase "comprising" in appellants' claimed invention results in appellants claiming a large genus of nucleic acid molecules which are not adequately described by SEQ ID NO: 1 through SEQ ID NO: 5. Answer, pages 13-16. Apparently the examiner is of the opinion that the claimed invention should be limited to nucleic acid molecules as set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In response appellants argue (Brief, page 14, original footnote omitted),

Applicants have provided the nucleotide sequences required by the claims, i.e., SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5, and have thus established possession of the claimed invention. The fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences⁶ does not mean that [a]pplicants were any less in possession of the claimed nucleic acid molecules.

As discussed supra, as we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NO: 1

⁶ By way of examples appellants explain (Brief, bridging paragraph, pages 14-15) that the specification discloses, inter alia, the claimed nucleic acid molecules joined together with vectors, and other nucleic acids (e.g. fusion nucleic acid molecules) and detectable labels.

through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. We agree with appellants that they have provided an adequate written description of nucleic acid molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. That the claimed nucleic acid molecules may have other molecules attached to either, or both of their 5' or 3' ends does not diminish appellants' adequate written description of the nucleic acids molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5 as claimed.

Accordingly, we reverse the rejection of claim 1 under the written description provision of 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith)
William F. Smith)
Administrative Patent Judge)
Donald E. Adams) BOARD OF PATENT
Donald E. Adams)
Administrative Patent Judge) APPEALS AND)
Eric Grimes) INTERFERENCES)
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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

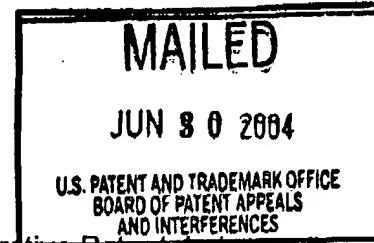
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

(15768)

Ex parte SCOTT E. ANDERSEN and JAMES D. MASUCCI

Appeal to C.A.F.C.
Docketed _____
Due Date 8/30/04 Application No. 09/540,232
Initial as _____

ON BRIEF



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

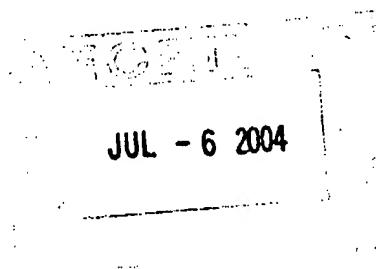
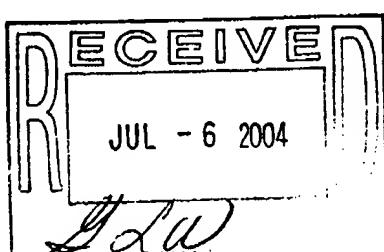
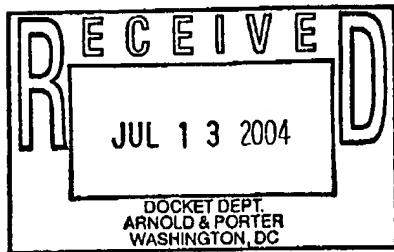
GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 2, the only claims remaining. The claims read as follows:

1. A substantially purified nucleic acid molecule that encodes a plant protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:93, SEQ ID NO:340, SEQ ID NO:1965, SEQ ID NO:1985, SEQ ID NO:1991, SEQ ID NO:1993, SEQ ID NO:4047, and SEQ ID NO:5683.

2. The substantially purified nucleic acid molecule according to claim 1, wherein said plant protein or fragment thereof is a lily protein or fragment thereof.



The examiner does not rely on any prior art.

Claims 1 and 2 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility.

Claims 1 and 2 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification.

We affirm the utility rejections and reverse the description rejection.

Background

The subject matter of the present appeal is directed to expressed sequence tags. "Expressed sequence tags, or ESTs, are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1.

As set forth at page 9 of the specification, "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a lily protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:6167." The specification discloses that these ESTs were obtained from cDNA libraries prepared from asiatic lily early ovary or late ovule tissue.

Pages 84-85.

The originally filed claims encompassed all of the 6167 disclosed sequences. On January 9, 2001 (Paper No. 4), the examiner entered a restriction requirement into the record, requiring appellants to elect, *inter alia*, up to ten nucleotide sequences for examination on the merits. Paper No. 4, page 2. In response, appellants elected SEQ ID Nos 78, 93, 340, 1954, 1965, 1985, 1991, 1993, 4047, and 5683. See Paper No. 5,

received Feb. 9, 2001. During prosecution, SEQ ID NO:1954 was deleted from the claims. See Paper No. 10, received Dec. 13, 2001.

The specification sets forth a number of utilities for the claimed nucleic acid molecules which are characterized by the examiner as "[g]eneral uses . . . includ[ing] acquiring genes, identifying polymorphisms, determining plant traits, and DNA mapping." Examiner's Answer, page 4. The examiner concluded that these uses do not establish patentable utility:

None of these [uses are] considered to be specific and substantial in view of the limited information provided in the specification. No plant traits are attributed to any SEQ ID NO. No complete gene is disclosed for any SEQ ID NO. No DNA maps or chromosomal locations are identified. No polymorphisms are identified. The specification does not disclose how a polymorphism would be recognized by those of ordinary skill in the art given the incomplete sequences disclosed.

Examiner's Answer, page 4.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See the Appeal Brief, pages 6-13. According to Appellants, "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, e.g., the ability to identify the presence or absence of a polymorphism in a population of lily plants." Id., page 3. Furthermore, appellants assert, "[t]he specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms." Id., page 8.

Discussion

1. Claim construction

As set forth above, claim 1 is directed to a "substantially purified nucleic acid molecule that encodes a plant protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:93, SEQ ID NO:340, SEQ ID NO:1965, SEQ ID NO:1985, SEQ ID NO:1991, SEQ ID NO:1993, SEQ ID NO:4047, and SEQ ID NO:5683." The specification defines "substantially purified" to mean

a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

Page 16, lines 12-18. As we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g., insertions or deletions) of the nucleotide sequences set forth in the recited SEQ ID NOs, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences of the recited SEQ ID NOs. Thus, claim 1 encompasses, inter alia, genes, full open reading frames, fusion constructs, and cDNAs.

The preamble of claim 1 also recites that the claimed nucleic acid "encodes a plant protein or fragment thereof." This phrase, however, merely recites an inherent function expected for the nucleotide sequences of the recited SEQ ID NOs; since the recited sequences were isolated as ESTs from lily tissue, they would be expected to

encode (parts of) lily proteins. Since the introductory phrase does not further limit the invention defined by the body of the claim, it is irrelevant to construction of the claim.

See IMS Technology, Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434, 54 USPQ2d 1129, 1137 (Fed. Cir. 2000) (“If the preamble adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim.”).

Accordingly, we interpret claim 1 as directed to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:93, SEQ ID NO:340, SEQ ID NO:1965, SEQ ID NO:1985, SEQ ID NO:1991, SEQ ID NO:1993, SEQ ID NO:4047, and SEQ ID NO:5683, with or without any preceding or trailing nucleotides or other molecules.

2. Utility

The starting point for determining whether the claimed nucleic acid molecules possess utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to “a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced.” Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that “where a claimed process produces a known product it is not necessary to show utility for the product.” Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.¹

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there

is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroid research and in the application of steroid materials to

¹ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only

that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" *Id.* at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." *Id.* The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. *Id.* "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." *Id.*

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." *Id.*, 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," *id.* at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[i]t is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.” Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court “perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question.” Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by “marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility.” Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at

1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal; i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We will focus on these asserted utilities first.

a. Polymorphisms

This utility is discussed at pages 38-45 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecules depicted in any of the SEQ ID NOs recited in claim

1. To the contrary, according to the specification, "one or more of the [6167] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify . . . polymorphism(s)." Page 35, lines 25-26. The specification does not explain why any of the 6167 nucleic acid molecules disclosed in the specification, or more specifically the nine nucleotide molecules depicted in SEQ ID NOs 78, 93, 340, 1965, 1985, 1991, 1993, 4047, and 5683, would in fact be useful in detecting polymorphisms.

Rather, Appellants argue that "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." Appeal Brief, page 8. In other words, Appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains,

[a] "polymorphism" is a collective concept defined by at least two variants (or alleles) found within members of a species collectively. Thus, one detects the presence of a polymorphism by analyzing multiple members of the species, i.e. analyzing a population. . . . The specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. . . .

The specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphism that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest.

Examiner's Answer, pages 11-12. In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene

and its role in the plant's development and/or phenotype lies the line that defines "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms." Appeal Brief, page 8. That may be true, but it does not show the patentable utility of the claimed nucleic acids, because the nucleic acids isolated from other plants have no apparent, substantial use. Again, the present specification does not attribute any property in terms of plant trait or phenotype to any of the nucleic acid molecules set forth in the SEQ ID NOs recited in claim 1. In the absence of such information, nucleic acids from other plants that hybridize to the claimed nucleic acids themselves lack substantial utility. Thus, the use of the claimed nucleic acids to isolate such nucleic acids does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Appeal Brief, pages 9-10. According to Appellants,

[t]he claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in ovary tissues at early and late stages of development. Isolation of such a promoter would be desirable and particularly useful because it allows expression of proteins at important developmental states, including proteins that provide increased reproductive ability. Because the claimed nucleic acid molecules were isolated from ovary tissue, they provide an appropriate starting point for isolating a promoter active in ovary tissue. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter.

Id., page 10. As we understand it, Appellants' argument is that the claimed ESTs may be useful in searching for promoters that are only active in ovary tissue. The specification, however, fails to demonstrate that any of the nucleic acid molecules set forth in the SEQ ID NOs recited in claim 1 would be useful in obtaining a successful result from such a search. The specification states that

[t]he [6167] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced[,] tissue specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 6167 nucleic acid molecules disclosed in the specification, or more specifically the nine nucleic acid molecules depicted in the SEQ ID NOs of claim 1, to isolate promoters of tissue-enhanced, tissue-specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles.

Furthermore, notwithstanding Appellants' assertion (Brief, page 10), there is no evidence on this record that any of the nucleic acid molecules recited in claim 1 are expressed in a tissue- or cell-type specific manner, or are developmentally or environmentally regulated. In this regard, we note that the claimed nucleic acid molecules were isolated from the cDNA libraries LIB3102 and LIB3103. Specification, pages 84-85. There is no evidence on this record that either of these libraries is a subtractive cDNA library, wherein nucleic acid molecules from other lily tissue, or from other developmental stages, was subtracted (removed) from the library. Thus, the cDNAs in the libraries LIB3102 and LIB3103 would be expected to include genes that

are expressed in a variety of lily tissues (e.g., genes involved in basic cell metabolism, synthesis of amino acids and other cellular components, and genes encoding ubiquitous structural proteins).

In our opinion, the claimed nucleic acid molecules having the sequences identified as SEQ ID NOs 78, 93, 340, 1965, 1985, 1991, 1993, 4047, and 5683, represent nine randomly selected nucleic acid molecules isolated from lily ovary tissue. Despite Appellants' assertion to the contrary, there is no reasonable expectation that any of the claimed nucleic acid molecules would be capable of isolating a promoter that was only active in ovary tissue. As Appellants recognize (Brief, page 10), "[a] random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter" compared to a nucleic acid molecule that is known to be specifically associated with this stage of plant development.

It is true, as Appellants argue, that "[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.'" Appeal Brief, page 10. However, with Appellants' claimed invention, there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See Brenner, 383 U.S. at 534, 148 USPQ at 695.

Appellants argue that the claimed nucleotide sequences are no less useful just because other nucleic acids can also be used to isolate promoters. See the Appeal Brief, page 9: "[T]he Examiner suggests that the asserted utilities are legally insufficient

simply because other molecules can be used for the same purpose. This position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law."

This argument is not persuasive. Appellants have never been asked to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, Appellants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form.).

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics.

On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

Here, Appellants argue that asserted "chromosome walking" utility would support patentability even if the claimed nucleic acid molecules were less useful for this purpose

than a totally random nucleotide sequence. Appeal Brief, page 10 ("[E]ven if a random nucleic acid provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules."). Clearly, the asserted utility is not based on the specific properties of the claimed nucleic acid molecules.

c. Other arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Appeal Brief, page 6. Specifically, Appellants argue (*id.*) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which, they assert, has a "legally sufficient utility." *Id.*

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (pages 75-78) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular

markers. Appeal Brief, page 6. In regard to microarrays, Appellants argue (*id.*, n.2) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that this asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in, e.g., SEQ ID NO:78. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification provides no guidance regarding what the SEQ ID NO:78-specific information derived from a gene expression experiment would mean. As the examiner points out, "further experimentation is required to identify a 'real world use.' . . . A positive result to such a screen requires further experimentation to determine what, if anything, such a change means." Examiner's Answer, page 9.

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO:78 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO:78 expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), or the degree of increase? The specification provides

The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands, even if the thousands of data points collectively are useful, does not meet this standard.

We also conclude that § 101's utility requirement is not satisfied by Appellants' assertion that the claimed nucleic acid molecules are useful as molecular markers or probes. Again, using one of the claimed nucleic acids as a molecular marker or probe to hybridize to part of a lily chromosome merely generates a single, uncharacterized data point that is useful only when combined with thousands of other data points. For the reasons discussed above in regard to gene expression assays, such uses do not represent "substantial" utility, as required by Brenner.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Appeal Brief, page 12. Since Appellants fail to provide any suggestion of which use of ESTs this industry is premised on, we can only assume that Appellants are referring to the potential usefulness of EST databases, clone sets, or microarrays. The claims on appeal, however, are not directed to EST databases, clone sets, or microarrays, but to individual, uncharacterized ESTs. Again, we do not agree that the one data point which

may be provided by using the uncharacterized nucleic acid molecules of claim 1 in such devices represents a substantial use.

In addition, it is reasonable to expect that the rule Appellants proffer – that ESTs are individually patentable because they are useful in gene expression assays – would hurt, rather than help, what they characterize as a “multi-million dollar industry in the United States premised on the usefulness of ESTs.” Under Appellants’ standard, any EST from most (if not all) organisms would be held to have patentable utility based on its use in generating gene expression data.² The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating all of the DNA sequences on the microarray to ensure that they were not the subject of someone else’s patent.

For each of the DNAs that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a “tragedy of the anticommons”:³

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex

² We can take judicial notice of the fact that organisms are of interest for many different reasons, such that gene expression assays could conceivably be used in their research. Humans, of course, are of interest in medical research. Other organisms are of interest to researchers because they have been historically well-studied (e.g., yeast, Arabidopsis, Drosophila), or because they are used as animal models for testing pharmaceuticals (e.g., mice, chimpanzees, rabbits), or because they are commercially valuable (e.g., pigs, corn, tomatoes), or because they are pests (e.g., Fusarium, ragweed, corn borers, zebra mussels), or because they are pathogens (e.g., Candida, various bacteria, tapeworms).

³ Heller et al., “Can patents deter innovation? The anticommons in biomedical research,” Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859). . . . To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. We therefore affirm the rejection of claim 1 under 35 U.S.C. § 101.

Claim 2 falls with claim 1. See the Appeal Brief, page 3.

3. Enablement

The examiner rejected claims 1 and 2 under 35 U.S.C. § 112, first paragraph, on the basis that "since the claimed invention is not supported by either a credible, specific, and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." Examiner's Answer, page 5. This rejection is simply a corollary of the finding of lack of utility.

Appellants argue that “[t]his rejection has been overcome by the arguments stated above regarding utility.” Appeal Brief, page 14. We do not agree that Appellants’ arguments overcome the rejection for lack of utility. Thus, our conclusion with respect to the § 101 issue also applies to the nonenablement rejection. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

4. Written description

The examiner rejected claims 1 and 2 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, reasoning that

[c]laim 1 is directed to a nucleic acid molecule “that encodes a plant protein or fragment thereof comprising.” The specification fails to describe any open reading frames, start/stop codons, or encoded proteins for any SEQ ID NO. As such, these nucleic acid molecules are not described. At best, the SEQ ID NOS. may include a sequence encoding a fragment but not a full length protein.

The use of the term “comprising” is interpreted to encompass full length proteins and gene sequences that have not been disclosed. The common structural features of these encoded plant proteins or fragments are not disclosed and thus the claimed subject matter cannot be considered as being described.

The specification describes only the particular SEQ ID NOS. and no longer sequences containing them. One can only envision the particular sequence disclosed and cannot envision any encoded protein sequence or larger sequences in which the claimed SEQ ID NOS. are embedded.

Examiner’s Answer, pages 5-6.

As we understand it, the examiner’s rejection has two bases. First, the claimed nucleic acids are not adequately described because the preamble of claim 1 states that the each of the nucleic acids “encodes a plant protein or fragment thereof,” and the specification does not describe any encoded proteins.

We will not sustain the rejection on this basis. The claims are directed to nucleic acids, not proteins, and the specification describes the complete sequence of each of the SEQ ID NOs that define the scope of the claimed nucleic acids. In addition, as we have construed the claims, the phrase that the examiner objects to ("encodes a plant protein or fragment thereof") has no patentable weight because it merely recites an inherent property that is expected for the claimed nucleic acids, based on the method by which they were isolated.

The second basis of the rejection, as we understand it, is that because of the transitional phrase "comprising", the claims encompass a large genus of nucleic acid molecules which are not adequately described by the SEQ ID NOs recited in the claim. See the Examiner's Answer, pages 18-20. Apparently, the examiner is of the opinion that the claimed invention should be limited to the nucleic acid molecules set forth in the recited SEQ ID NOs.

In response, Appellants argue that "[t]he fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences does not mean that Applicants were any less in possession of the claimed nucleic acid molecules." Appeal Brief, page 16.

We have interpreted the claims to allow for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in the recited SEQ ID NOs, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences of the recited SEQ ID NOs. See pages 4-5, supra. We agree with Appellants that the claims, so interpreted, are supported by an adequate written description in the specification. The fact that the claimed nucleic acid molecules may

have other molecules attached to either or both of their 5' or 3' ends does not diminish Appellants' adequate written description of the nucleic acids molecules with the sequences set forth in the recited SEQ ID NOs, as claimed.

Accordingly, we reverse the rejection of claims 1 and 2 for lack of adequate written description.

Summary

Although we reverse the examiner's rejection for lack of adequate written description, we affirm the rejection of claims 1 and 2 for lack of patentable utility.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

WILLIAM F. SMITH)
Administrative Patent Judge)
DONALD E. ADAMS) BOARD OF PATENT
Administrative Patent Judge)
ERIC GRIMES) APPEALS AND
Administrative Patent Judge) INTERFERENCES

Appeal No. 2003-1
Application No. 09/540,232

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 25



UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JOSEPH R. BYRUM,
GREGORY R. HECK, and THOMAS J. LA ROSA

Appeal No. 2003-1504
Application No. 09/440,687

ON BRIEF¹

MAILED

JUN 30 2004

U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

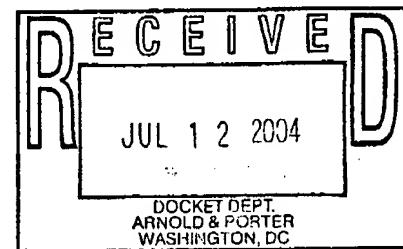
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 8-19. Claim 1 is illustrative of the subject matter on appeal and is reproduced below.

1. A substantially purified nucleic acid molecule that encodes a soybean protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10.

The examiner does not rely on a reference.



¹ Appellants waived their request for oral hearing. Paper No. 24. Accordingly, we considered this appeal on Brief.

GROUNDS OF REJECTION

Claims 1 and 8-19 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility.

Claims 1 and 8-18 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification that fails to adequately describe the claimed invention.

We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph and reverse the written description rejection under 35 U.S.C. § 112, first paragraph.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags. "Expressed sequence tags, or ESTs, are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones."

Specification, page 1.

According to appellants (*id.*), "[t]he invention relates to nucleic acid molecules that encode proteins and fragments of proteins produced in plant cells, in particular, soybean plants." More particularly, appellants disclose "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a soybean protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 31[.]015." Specification, page 9.

Of the 31,015 sequences disclosed in appellants' specification, the original claims filed with the application were directed to nucleic acid molecules that comprise a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1 – 4,486. On May 25, 2000 (Paper No. 4), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants to elect up to 10 independent and distinct nucleotide sequences. Paper No. 4, bridging paragraph, pages 2-3. In response, appellants elected SEQ ID NOs: 1-10². Paper No. 5, page 2.

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a soybean protein or fragment thereof comprising nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10. According to appellants' specification (bridging paragraph, pages 16-17), the term "substantially purified" refers

to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

² Appellants disclose (specification, page 87), SEQ ID NO: 1 through SEQ ID NO: 4486 were obtained from the cDNA library LIB3040 which was "generated from soybean cultivar Asgrow 3244...."

As we understand the subject matter of claim 1, the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NOs: 1-10, but instead only allows for the addition of nucleotides or other molecules³ at either end of the nucleotide sequences.

In this regard, we recognize, as does the examiner (Answer, page 7), "[t]he claims encompass the nucleic acid for the gene (including introns and other non-coding information)...." For example, as explained by appellants (Brief, page 14),

[t]he present application describes more than just the nucleotide sequence required by the claims (SEQ ID NOs: 1 through 10), for example, it describes vectors comprising the claimed nucleic acid molecules ... [and] the addition of extra nucleotides or detectable labels to the disclosed nucleotide sequences.

The preamble of claim 1 also recites that the claimed nucleic acid molecule "encodes a soybean protein or fragment thereof." This phrase, however, merely recites an inherent function expected for the nucleic acid molecule defined by the SEQ ID NOs set forth in the claim; since the recited sequences were isolated as ESTs from soybean tissue, they would be expected to encode (parts of) soybean proteins. Since the introductory phrase does not further limit the invention defined by the body of the claim, it is irrelevant to construction of the claim. See IMS Technology, Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434, 54 USPQ2d 1129, 1137 (Fed. Cir. 2000) ("If the preamble

³ According to appellants' specification (page 17), "agents of the present invention may be labeled with reagents that facilitate detection of the agent (e.g., fluorescent labels, ... chemical labels, ... [and] modified bases...."

adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim.").

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10, with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether the nucleic acid molecule of claim 1⁴ possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695⁵,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

⁴ According to appellants (Brief, page 3), "[p]atentability of claims 1 and 8-19 is addressed together..." We interpret this statement to mean that claims 1 and 8-19 stand or fall together. Accordingly, we limit our discussion to representative independent claim 1. Claims 8-19 will stand or fall together with claim 1. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

⁵ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1563-64, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁶

The Court, finding “no specific assistance in the legislative materials underlying § 101,” based its analysis on “the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.” Id. at 532, 148 USPQ at 695. The Court concluded that “[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant’s argument that attenuating the requirement of utility “would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge.” The Court noted that, while there is value to encouraging disclosure, “a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast,

⁶ The invention at issue in Brenner was a process, but the Court expressly noted that its holding “would apply equally to the patenting of the product produced by the process.” Id. at 535, 148

unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroid research and in the application of steroid materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help

their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a

rejection based on an intervening reference. Id. “[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there.”

Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were “well recognized in the art as valuable for use in cancer chemotherapy.” Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were “relevant to the treatment of humans and [were] not to be disregarded,” id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention

has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk,

376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

On this record, appellants assert (Brief, bridging paragraph, pages 5-6, footnotes omitted) that the specification sets forth a number of utilities for the claimed nucleic acid molecule

e.g., to detect the presence and/or identity of polymorphisms, and as hybridization probes for expression profiling ... [in addition to introducing] the claimed nucleic acid molecules into a plant or plant cell (as antisense inhibitors), which can then be used to screen for compounds such as a herbicide ... to measure the level of mRNA in a sample, and use as molecular markers.

We note, however, that the specification does not specifically disclose how to use a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10, as set forth in claim 1. To the contrary, the specification describes the aforementioned utilities as applicable to all of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 31,015. See e.g., specification, pages 9-15. We note, however, that appellants discuss the potential activity of populations of nucleic acid molecules that includes less than all 31,015 nucleic acid sequences. See specification, pages 32-35. This section describes the cDNA libraries from which specific populations of nucleotide sequences were obtained. As discussed supra, SEQ ID NO: 1 through SEQ ID NO: 4,486 were obtained from the cDNA

library LIB3040. Specification, page 87. According to appellants' specification (bridging paragraph, pages 32-33),

[t]he ESTs of ... [the LIB3040] library can enable acquisition of, but are not limited to, genes involved in seed development, therefore, the ESTs of the present invention will also find great use in the isolation of a variety of agronomically significant genes, including but not limited to genes that regulate proteins, amino acids, sterols, oils, minerals, isoflavones, saponins, trypsin inhibitors, vitamins, tocopherols, antinutrient components, carbohydrates, starch metabolism, and seed regulatory elements. Such genes are associated with plant growth, quality, yield, and could also serve as links in important metabolic, developmental and catabolic pathways.

Appellants, however, fail to disclose which of the aforementioned activities, if any, can be attributed to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10.

Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 40-47 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecule set forth in claim 1. To the contrary, according to appellants' specification (e.g., page 46, lines 15-16), "one or more of the [31,015] nucleic acids of the present invention, may be utilized as markers or probes to detect polymorphisms...."

The specification does not explain why any of the 31,015 nucleic acid molecules disclosed in the specification, or more specifically a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 10 would in fact be useful in detecting polymorphisms. Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that a nucleic acid by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. See e.g., Brief, page 10. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleic acid, as here, detection of the presence or absence of a

polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, page 12), appellants' specification defines "polymorphism" as

"a variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species." It follows from this definition that if there is no "variation or difference in the sequence of the gene or its flanking regions" among "members of a species," then no polymorphism exists, i.e. a polymorphism is absent, in this region of the genome.

According to the examiner (Answer, page 11), "the presence or absence of any of the claimed nucleotide sequences in a sample (or polymorphisms thereof) has no meaning absent some association. Further experimentation is required to determine what, if any, that meaning or association might be." In this regard, the examiner finds (Answer, page 12), appellants' specification "does not disclose whether the claimed nucleic acid molecules can, if fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves open the possibility that there may be no polymorphism to detect." According to the examiner (Answer, bridging paragraph, pages 12-13), "[t]he specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest." According to the examiner (Answer, page 14), "the specification fails to identify even one specific polymorphism that can be detected with the claimed nucleic acid molecule, the specification fails to show any specific correspondence between the disclosed general utility and the claimed subject matter, regardless of any specific application requiring detection of polymorphisms." Accordingly the examiner finds (id.), "using the claimed

invention to first determine whether or not the claimed nucleic acid molecule can, in fact, detect a polymorphism is to determine whether or not the claimed invention has a utility that requires detecting a polymorphism, i.e. it is 'use testing' and not substantial."

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the nucleic acid is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.⁷

b. Probes or source of primers

Appellants assert that the "specification discloses that the claimed nucleic acid molecules can be used ... to isolate nucleic acid molecules of other plants and organisms...." Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or

⁷ For the foregoing reasons, we disagree with appellants' assertion (Brief, page 3) that the claimed nucleic acid molecule provides "at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism."

phenotype to the nucleic acid molecule set forth in claim 1. In the absence of such information, using the claimed molecule to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.⁸

Appellants also assert that the claimed nucleic acid molecule may be used in a "chromosome walk." Brief, page 8. According to appellants (Brief, page 9),

The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in soybean. ... A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

As we understand this argument, the claimed nucleic acid may be useful in searching for promoters that are active in soybeans. The specification, however, fails to demonstrate that a nucleic acid molecule as set forth in claim 1 would be useful in obtaining a successful result from such a search. As set forth at page 38, lines 15-20 of appellants' specification,

The [31,015] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell -type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

⁸ In addition, we note the examiner's assertion (Answer, page 16), "[a]t the time the application had been filed, future experimentation on the part of one skilled in the art would have been required to determine which, if any, other plant species contained nucleic acid molecules that could have been obtained using the claimed invention, and under what experimental conditions."

The specification does not provide any expectation of successfully using any of the 31,015 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid molecule of claim 1 to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles. According to the examiner (Answer, page 16), "the specification fails to disclose any characteristics of the corresponding promoter, or any other promoter within 'chromosome walking' distance; neither structural characteristics, by which the promoter might be identified, nor functional characteristics, by which a specific and substantial use for the promoter might be determined." By way of example, the examiner argues (Answer, page 17), assume

a nucleotide sequence is identified during the chromosome walk as a putative promoter by sequence analysis, is then subcloned into operable linkage with a reporter gene and transfected into an appropriate cell, but found not to express the reporter gene in the cells. This result could mean the putative promoter: is not truly a promoter, i.e. a false positive; is not the corresponding promoter; or is incomplete, i.e. lacked additional sequence elements required for promoter activity in the seed pod cells.

According to the examiner (Answer, page 11), appellants merely isolated the claimed nucleic acid molecule, "[t]hey have not tested, evaluated, or calibrated the claimed nucleotide sequence for any particular use."

We recognize appellants' argument (Brief, page 9), "[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986)." While we agree with appellants' statement, we fail to see how it applies to appellants' claimed

invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Brief,

page 5. Specifically, appellants argue (*id.*) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." *Id.*

However, the examiner finds (Answer, page 9), further research is required to use the claimed nucleic acid molecules "to detect the presence and/or identity of polymorphisms, as hybridization probes for expression profiling, as antisense inhibitors by introduction of the claimed nucleic acid molecule into a plant or plant cell where the resulting cell or plant is to be used to screen compounds such as herbicides, to measure the level of mRNA in a sample, and as a molecular marker." In addition, the examiner finds (*id.*), that since targets are not disclosed in the specification, the use of the claimed nucleic acid molecule "as antisense inhibitors would require further experimentation to determine the target of inhibition." To the extent that appellants would argue that the claimed nucleic acid could be used in assays that measure the presence of a material that correlates to a predisposed disease condition, the examiner finds (Answer, page 7), "[t]he instant specification sets forth no such correlation for any condition."

As to the use of the claimed nucleic acid in microarrays (see e.g., Brief, page 6, n. 4), the examiner finds (Answer, page 10), "[a]ppellant is [sic] not claiming microarrays or collections of nucleotides and the specification does not

associate the claimed sequence with any trait of interest." According to the examiner (Answer, page 10),

[c]ontrary to appellant's [sic] assertions, further experimentation is required to identify a "real world use." A negative result to such a screen tells what the nucleic acid is not and cannot be used for. A positive result to such a screen requires further experimentation to determine what, if anything, such a change means. It is not an immediate benefit except in the sense to indicate that further research might yield a "real world use."

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. In regard to microarrays, we find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid molecule set forth in claim 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the specific information derived from a gene expression experiment would mean in the context of a nucleic acid molecule as set forth in claim 1.

To highlight the examiner's assertion (Answer, page 10), suppose, for example, that a researcher found that expression of the nucleic acid molecule set forth in claim 1 was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to

determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the nucleic acid molecule of claim 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use the specific gene expression data in the context of the nucleic acid molecule of claim 1.

Assuming arguendo, that a generic gene expression assay - one based on monitoring expression of thousands of uncharacterized nucleic acids - would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid - its data point - is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the

applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecule set forth in claim 1 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 10. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 1 in such devices represents a substantial use.

Further, we understand appellants' position to be that a compound would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

Not only is appellants' proposed utility standard contrary to controlling case law, but there are reasons to expect that it would hurt – rather than help – the microarray industry. Under appellants' standard, any naturally occurring gene, and fragments thereof, would be held to have patentable utility based on its use in generating expression data. The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating the patent status of each oligonucleotide on the microarray. Not only that, but since appellants assert that their reasoning supports the utility of gene fragments, all of the subsequences of each of the genes would have to be checked to ensure that they were not the subject of someone else's patent.

For each of the genes (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons":⁹

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the

⁹ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," *Science*, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859).... To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

We note that the examiner acknowledges appellants' assertion (Brief, page 5, n. 2), "[i]t is irrelevant whether the corresponding mRNA or polypeptide have utility because [a]pplicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules." Answer, page 8. Nevertheless, the examiner asserts (Answer, bridging sentence, pages 8-9), "[t]he [B]rief does not dispute that no open reading frame (ORF), no encoded protein, nor any biological activity for any encoded protein has been disclosed for SEQ ID NOS: 1-10."

As for non-asserted utilities, the examiner finds (Answer, page 6), "there is no evidence of a well-established utility for the disclosed ESTs or claimed nucleic acid molecules."

The basic quid pro quo of the patent system requires disclosure of an invention having substantial utility. On reflection, we find appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101. For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101. As discussed supra, claims 8-19 fall together with claim 1.

Enablement

According to the examiner (Answer, page 6), "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), "[t]his rejection was erroneous and has been overcome by the arguments stated above regarding ... [the rejection under 35 U.S.C. § 101]." Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph. As discussed supra, claims 8-19 fall together with claim 1.

Written description

The examiner rejected claims 1 and 8-18 under 35 U.S.C. § 112, first paragraph, for lack of an adequate written description. According to the examiner (Answer, page 7),

[t]he claims encompass the nucleic acid for the gene (including introns and other non-coding information) within the scope of the invention by virtue of the "comprising" and "encoding" language. ... Neither the structural and functional properties of any gene comprising SEQ ID NOS: 1-10 nor the structural and functional properties of any protein or fragment thereof encoded by a nucleotide sequence comprising SEQ ID NOS: 1-10 are disclosed in the specification.

As we understand it, the examiner's rejection has two bases. First, the claimed nucleic acids are not adequately described because the preamble of claim 1 states that the claimed nucleic acid molecule "encodes a soybean protein or fragment thereof," and the specification does not describe any encoded proteins.

We will not sustain the rejection on this basis. The claims are directed to nucleic acid molecules, not proteins, and the specification describes the complete sequence of each of the SEQ ID NOs that define the scope of the claimed nucleic acid molecules. In addition, as we have construed the claims, the phrase that the examiner objects to ("encodes a soybean protein or fragment thereof") has no patentable weight because it merely recites an inherent property that is expected for the claimed nucleic acids, based on the method by which they were isolated.

The second basis of the rejection, as we understand it, is that because of the transitional phrase "comprising", the claims encompass a large genus of

nucleic acid molecules, which are not adequately described by the SEQ ID NOs recited in the claim. See Answer, pages 19-22. Apparently, the examiner is of the opinion that the claimed invention should be limited to the nucleic acid molecules set forth in the recited SEQ ID NOs.

We have interpreted the claims to allow for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in the recited SEQ ID NOs, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences of the recited SEQ ID NOs. See pages 3-5, supra. The fact that the claimed nucleic acid molecules may have other molecules attached to either or both of their 5' or 3' ends does not diminish Appellants' adequate written description of the nucleic acids molecules with the sequences set forth in the recited SEQ ID NOs, as claimed.

Accordingly, we reverse the rejection of claims 1 and 8-18 for lack of adequate written description.

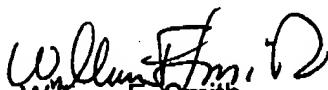
Summary

We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph.

We reverse the written description rejection under 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED


William F. Smith
Administrative Patent Judge


Donald E. Adams
Administrative Patent Judge


Eric Grimes
Administrative Patent Judge

)
) BOARD OF PATENT
)
) APPEALS AND
)
) INTERFERENCES
)

Lawrence M. Lavin, Jr.
Monsanto Company
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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 25

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MARK S. ABAD and THOMAS J. LA ROSA

Appeal No. 2003-1135
Application No. 09/565,240

ON BRIEF¹

MAILED

JUN 30 2004

U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

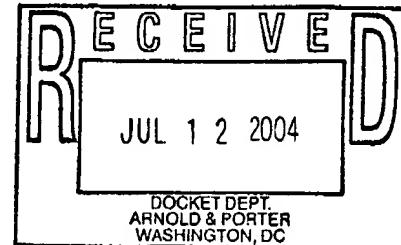
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 1, which is reproduced below.

1. A substantially purified nucleic acid molecule that encodes a soybean protein or soybean protein fragment comprising the nucleic acid sequence of SEQ ID NO: 49441.

The examiner does not rely on a reference.



¹ Appellants waived their request for oral hearing. Paper No. 24. Accordingly, we considered this appeal on Brief.

GROUNDS OF REJECTION

Claim 1 stands rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. We affirm.

BACKGROUND

According to appellants' specification (page 1), "[t]he invention relates to nucleic acid molecules that encode proteins and fragments of proteins produced in plant cells, in particular, soybean plants." More particularly, appellants disclose "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a soybean protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 54[,]005." Specification, page 9.

Of the 54,005 sequences disclosed in appellants' specification, the original claims filed with the application were directed to nucleic acid molecules that comprise a nucleic acid sequence selected from the group consisting of SEQ ID Nos: 49,441 – 54,005. On February 9, 2001 (Paper No. 2), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants to elect a single nucleic acid sequence for consideration on the merits. Paper No. 2, page 2. In response, appellants elected SEQ ID NO: 49,441². Paper No. 5, page 2.

² Appellants disclose (specification, page 98, as amended in Paper No. 11, pages 8-9), SEQ ID NO: 49,441 was obtained from the cDNA library LIB3167.

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a soybean protein or soybean protein fragment comprising the nucleic acid sequence set forth in SEQ ID NO: 49,441.

According to appellants' specification (page 17), the term "substantially purified"

refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the subject matter of claim 1 the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NO: 49,441, but instead only allows for the addition of nucleotides or other molecules³ at either end of the nucleotide sequence set forth in SEQ ID NO: 49,441. In this regard, we recognize, as does the examiner (Answer, page 4), the claim as written encompasses, inter alia, any full length gene, fusion construct, RNA or cDNA that comprises the nucleotide sequence set forth in SEQ ID NO: 49,441 and is capable of encoding at least a fragment of a soybean protein.

³ According to appellants' specification (page 17), "agents of the present invention may be labeled with reagents that facilitate detection of the agent (e.g., fluorescent labels, ... chemical labels, ... [and] modified bases...")

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that comprises the nucleotide sequence set forth in SEQ ID NO: 49,441 with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether the nucleic acid molecule of claim 1 possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695⁴,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point—where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C.

⁴ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1563-64, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

§ 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[I]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁵

⁵ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroid research and in the application of steroid materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties' did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the

first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are.” Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. “There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of ‘useful in research’ or ‘useful as building blocks of value to the researcher’ was recognized, and clearly rejected, by the Supreme Court” in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. “In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was ‘plastic-like.’” Id. at 1203, 26 USPQ2d at 1605. “Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility.” Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. “[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of

the German application; but in that application Ziegler had not yet gotten there.”

Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were “well recognized in the art as valuable for use in cancer chemotherapy.” Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were “relevant to the treatment of humans and [were] not to be disregarded,” id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that “[it] is axiomatic that an invention cannot be considered ‘useful,’ in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious.” Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court “perceive[d] no

insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk,

376 F.2d at 945, 153 USPQ at 55 (*interpreting Brenner*). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

On this record, appellants assert (Brief, bridging paragraph, pages 5-6) that specification sets forth a number of utilities for the

present invention, including "probes for assisting in the isolation of full-length cDNAs or genes which would be used to make protein and optionally further usage to make the corresponding antibodies, gene mapping, isolation of homologous sequences, detection of gene expression such as in Northern blot analysis, molecular weight markers, chromosomal markers, and for numerous other generic genetic engineering usages." ... In addition to ... detecting the presence and level of mRNA in a sample; identifying polymorphisms; obtaining promoters and other flanking genetic elements to such molecules; determining the location of a corresponding DNA sequence on a genetic map; isolating related nucleic acid and protein molecules; and conducting plant transformation or transfection; etc....

We note, however, that the specification does not specifically disclose how to use a nucleic acid molecule comprising the nucleic acid sequence set forth in SEQ ID NO: 49,441, as set forth in claim 1. To the contrary, the specification describes the aforementioned utilities as applicable to all of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 54,005. See e.g., specification, pages 9-15. We note, however, that appellants discuss the potential activity of (specification, pages 33-39) populations of nucleic acid molecules that includes less than all 54,005 nucleic acid sequences. This section describes the cDNA libraries from which specific populations of

nucleotide sequences were obtained. As discussed supra, SEQ ID NO: 49,441 through SEQ ID NO: 54,005 were obtained from the cDNA library LIB3167. Specification, page 98, as amended in Paper No. 11, pages 8-9. According to appellants' specification (bridging paragraph, pages 38-39),

the [LIB3167] cDNA library of the present invention can enable acquisition of, including but not limited to, stress response genes and genes that regulate PR proteins ... the ESTs of the present invention will also find great use in the isolation of a variety of agronomically significant genes, including but not limited to genes that regulate germination, developmental stress, protein, amino acids, sterols, oils, minerals, isoflavones, saponins, trypsin inhibitors, vitamins, tocopherols, antinutrient components, carbohydrates, starch metabolism, and seedling and vegetative regulatory elements. Such genes are associated with plant growth, quality, yield, and could also serve as links in important metabolic, developmental and catabolic pathways.

Appellants, however, fail to disclose which of the aforementioned activities, if any, can be attributed to the nucleic acid molecule comprising the sequence set forth in SEQ ID NO: 49,441, or a protein or protein fragment encoded thereby.

Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 43-55 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however,

is not specific to the nucleotide molecule set forth in claim 1. To the contrary, according to appellants' specification (e.g., page 50, lines 7-9), "one or more of the [54,005] nucleic acids of the present invention, may be utilized as markers or probes to detect polymorphisms...."

The specification does not explain why any of the 54,005 nucleic acid molecules disclosed in the specification, or more specifically a nucleic acid molecule comprising the nucleic acid sequence set forth in SEQ ID NO: 49,441 would in fact be useful in detecting polymorphisms. Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that a nucleic acid by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. See e.g., Brief, page 10. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by the nucleic acid, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, page 7),

While agreement is reached in that some polymorphisms have been found to be useful as a result of their presence having been correlated with another event, e.g., the development of cancer in an individual, the over or under expression of one or more genes that has in turn a specific effect that has known value. In the

present case, however, the claimed nucleic acid sequence has not been tightly associated with any one protein. Indeed, the appellant is less than [sic] assured that the claimed nucleic acid encodes an intact protein or a fragment of a soybean protein....

Stated differently, whether the claimed nucleotide sequence is capable of detecting the presence or absence of a polymorphism has no meaning absent some association.

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the nucleic acid is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.⁶

b. Probes or source of primers

Appellants assert that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Brief, page 7. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or

⁶ For the foregoing reasons, we disagree with appellants' assertion (Brief, page 3) that the claimed nucleic acid molecule provides "at least one specific benefit to the public, e.g., the ability to identify the presence or absence of a polymorphism in a population of soybean plants."

phenotype to any of the nucleic acid molecule set forth in claim 1. In the absence of such information, using the claimed molecule to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk" or to isolate "the promoter of the gene corresponding to the claimed nucleic acid molecules." Brief, page 8. As we understand this argument, the claimed nucleic acid may be useful in searching for promoters. The specification, however, fails to demonstrate that the nucleic acid molecule set forth in claim 1 would be useful in obtaining a successful result from such a search. As set forth in appellants' specification (bridging paragraph, pages 41-42),

The [54,005] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell -type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification, however, does not provide any expectation of successfully using any of the 54,005 nucleic acid molecules disclosed in the specification, or more specifically the nucleic acid molecule of claim 1 to isolate promoters having cell enhanced, cell specific, tissue enhanced, tissue specific, developmentally or environmentally regulated expression profiles.

We agree with appellants' assertion (Brief, page 8) that an invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101. In this regard, we note the examiner's argument (Answer, page 8), "a review of the disclosure fails to find where any specific chromosome as being a target for initiating chromosome walking or for otherwise marking a specific region of interest of a given chromosome. Accordingly, the utility asserted is considered to be 'general' and not 'specific'."

c. Other Arguments

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only

assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. In regard to microarrays, we find that the use of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid molecule set forth in claim 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the specific information derived from a gene expression experiment would mean in the context of a nucleic acid molecule as set forth in claim 1.

Suppose, for example, that a researcher found that expression of the nucleic acid molecule set forth in claim 1 was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of

increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the nucleic acid molecule of claim 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use the specific gene expression data in the context of the nucleic acid molecule of claim 1.

Assuming arguendo, that a generic gene expression assay - one based on monitoring expression of thousands of uncharacterized nucleic acids - would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the

assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form.

Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard.

The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecules set forth in claim 1 are useful as a molecular marker or probe. It is not seen that the one data point that may be provided by using the

uncharacterized nucleic acid molecule of claim 1 as a molecular marker or probe represents a substantial use.

Further, we understand appellants' position to be that a compound would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

Not only is appellants' proposed utility standard contrary to controlling case law, but there are reasons to expect that it would hurt – rather than help – the microarray industry. Under appellants' standard, any naturally occurring gene or polypeptide, and fragments thereof, would be held to have patentable utility based on its use in generating expression data. The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating the patent status of each oligonucleotide on the microarray. Not only that, but since appellants assert that their reasoning supports the utility of gene and polypeptide fragments, all of the subsequences of each of the genes or polypeptides would have to be checked to ensure that it was not the subject of someone else's patent.

For each of the genes or polypeptides (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an

aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons":⁷

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859).... To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

The basic guid pro quo of the patent system requires disclosure of an invention having substantial utility. Appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101.

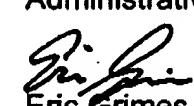
⁷ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101.

Enablement

According to the examiner (Answer, pages 5-6), "since the claimed invention is not supported by either a specific asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, bridging paragraph, pages 11-12), this rejection should be reversed for the same reasons set forth in their arguments regarding the rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

AFFIRMED

)
William F. Smith)
Administrative Patent Judge)
) BOARD OF PATENT
Donald E. Adams)
Administrative Patent Judge) APPEALS AND
)
Eric Grimes) INTERFERENCES
Administrative Patent Judge)

Lawrence M. Lavin, Jr.
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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

15746-6

Paper No. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RAGHUNATH V. LALGUDI,
PHILIP W. MILLER and KEITH O'CONNELL

Appeal No. 2003-0996
Application No. 09/540,215

ON BRIEF¹



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

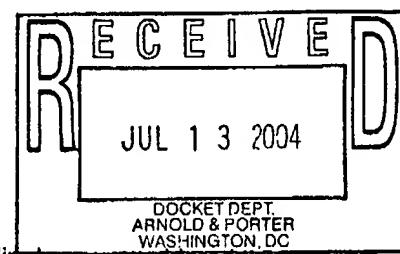
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 2 and 4-7. Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. A substantially purified nucleic acid molecule that encodes an algal protein or fragment thereof comprising the nucleic acid sequence of SEQ ID NO: 1.

The examiner does not rely on a reference.



¹ Appellants waived their request for oral hearing. Paper No. 20. Accordingly, we considered this appeal on Brief.

GROUNDS OF REJECTION

Claims 1, 2 and 4-7 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility.

Claims 1, 2 and 4-7 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification that fails to adequately describe the claimed invention.

We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph and reverse the written description rejection under 35 U.S.C. § 112, first paragraph.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags. "Expressed sequence tags, or ESTs, are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones."

Specification, page 3.

According to appellants' specification (page 1), "[t]he present invention relates to nucleic acid sequences from the unicellular green algae, Chlorella vulgaris.²¹" More particularly, appellants disclose "[t]he present invention provides a substantially purified nucleic acid molecule having a nucleic acid

² We note that while claim 2 on appeal is limited to a nucleic acid molecule that comprises SEQ ID NO: 1 and encodes a Chlorella vulgaris protein or fragment thereof, claim 1 on appeal is much broader in scope and encompasses a nucleic acid sequence that encodes any "algal protein or fragment" and comprises the sequence set forth in SEQ ID NO: 1.

sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 3,519." Specification, page 12.

The original claims filed with the application were directed to nucleic acid molecules that comprise a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1 – 3,519. On July 3, 2001 (Paper No. 5), the examiner entered a Restriction requirement into the record. According to the examiner (*id.* at page 3), "[e]xamination will be restricted to only the elected sequences. For the instant application, the nucleic acid sequences are considered to be complex and thus, election of a single SEQ ID Number is required." In response, appellants elected SEQ ID NO: 1. Paper No. 7, page 2.

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes an algal protein or fragment thereof comprising the nucleic acid sequence of SEQ ID NO: 1. According to appellants' specification (page 14), the term "substantially purified" refers

to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the subject matter of claim 1 the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence set forth in SEQ ID NO: 1, but instead only allows for the

addition of nucleotides or other molecules³ at either end of the nucleotide sequence.

The preamble of claim 1 also recites that the claimed nucleic acid molecule “encodes an algal protein or fragment thereof.” This phrase, however, merely recites an inherent function expected for the nucleotide sequence of the recited SEQ ID NO; since the recited sequence was isolated as an EST from Chlorella vulgaris C-265⁴, it would be expected to encode (part of) an algal protein. Since the introductory phrase does not further limit the invention defined by the body of the claim, it is irrelevant to construction of the claim. See IMS Technology, Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434, 54 USPQ2d 1129, 1137 (Fed. Cir. 2000) (“If the preamble adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim.”).

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, that comprises a nucleotide sequence of SEQ ID NO: 1, with or without any preceding or trailing nucleotides, or other molecules.

³ According to appellants' specification (page 15), “agents of the present invention may be labeled with reagents that facilitate detection of the agent (e.g., fluorescent labels, ... chemical labels, ... [and] modified bases....”

⁴ As set forth on page 109 of the specification “[t]he cDNA library LIB191 is prepared from the cultures of the eukaryotic green microalgae Chlorella vulgaris C-265.” At page 110 of the specification, appellants disclose that “[t]he ESTs of the present invention are generated by sequencing initiated from the 5' end of each cDNA clone.”

DISCUSSION

Utility

The starting point for determining whether the nucleic acid molecule of claim 1⁵ possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695⁶,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," *i.e.*, "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

⁵ According to appellants (Brief, page 3), "[t]he patentability of claims 1, 2 and 4-7 is addressed in Sections 8.A through 8.D...." We interpret this statement to mean that claims 1, 2 and 4-7 stand or fall together. Accordingly, we limit our discussion to representative independent claim 1. Claims 2 and 4-7 will stand or fall together with claim 1. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

⁶ In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1563-64, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

[I]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.⁷

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the

⁷ The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that

what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroid research and in the application of steroid materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there."

Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for

the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ing] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use"

that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a

practical utility for polypropylene at the time of the filing," but not yet there.

Ziegler, at 1203, 26 USPQ2d at 1605.

On this record, appellants assert (Brief, bridging paragraph, pages 5-6, footnotes omitted),

The instant specification describes multiple utilities for the present invention, including as probes in an array, to screen for polymorphisms, for gene mapping, and expressing protein for generating antibodies, etc. ... [in addition to] determining the [e]xpression [r]esponse of a green algae as a function of the mRNA levels expressed by the cells ... to identify polymorphisms, in addition to their use as molecular markers.

We note, however, that the specification does not specifically disclose how to use a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 1. To the contrary, the specification describes the aforementioned utilities as applicable to all of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 3,519. See e.g., specification, pages 12-13. Stated differently, the specification fails to disclose, with any degree of specificity, the utility of a nucleic acid molecule as claimed.

Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 93-101 of the specification in terms of what polymorphisms are and how one would go about determining the existence

of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecule set forth in claim 1. To the contrary, according to appellants' specification (e.g., page 94, lines 4-5), "one or more of the [3,519] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify ... polymorphism(s)."

The specification does not explain why any of the 3,519 nucleic acid molecules disclosed in the specification, or more specifically a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 1 would in fact be useful in detecting polymorphisms. Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that a nucleic acid by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. See e.g., Brief, page 10. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by a nucleic acid, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, page 11), appellants' specification defines

"polymorphism" as

a "variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species." (page 94). It follows from this definition that if there is no "variation or difference in the sequence of the gene or its flanking regions" among "members of a species," then no polymorphism exists, i.e. a polymorphism is absent, in this region of the genome.

According to the examiner (Answer, page 10), "the presence or absence of any of the claimed nucleotide sequences in a sample (or polymorphisms thereof) has no meaning absent some correlation to an immediate benefit." In this regard, the examiner finds (Answer, page 11), appellants' specification "does not disclose whether the claimed nucleic acid molecules can, if fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves open the possibility that there may be no polymorphism to detect." According to the examiner (Answer, page 12),

[t]he specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphisms that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest.

According to the examiner (Answer, page 13), "the specification fails to identify even one specific polymorphism that can be detected with the claimed nucleic acid molecule, the specification fails to show any specific correspondence between the disclosed general utility and the claimed subject matter, regardless of any specific application requiring detection of polymorphisms." Accordingly the examiner finds (id.), "using the claimed invention to first determine whether or

not the claimed nucleic acid molecule can, in fact, detect a polymorphism is to determine whether or not the claimed invention has a utility that requires detecting a polymorphism, i.e. it is 'use testing' and not substantial."

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the nucleic acid is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.⁶

b. Probes or source of primers

Appellants assert that the "specification discloses that the claimed nucleic acid molecules can be used ... to isolate nucleic acid molecules of other plants such as soybean, alfalfa, Arabidopsis, barley, maize, etc." Brief, page 8, footnote omitted. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to the nucleic acid molecule set forth in claim 1. In the absence of such information, using the

⁶ For the foregoing reasons, we disagree with appellants' assertion (Brief, page 3) that the claimed nucleic acid molecule provides "at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of algae."

claimed molecule to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.⁹

Appellants also assert that the claimed nucleic acid molecule may be used in a "chromosome walk." Brief, page 9. According to appellants (Brief, page 9),

The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in green algae. ... Random nucleic acid molecules are not similarly suitable. ... Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules.

As we understand this argument, the claimed nucleic acid may be useful in searching for promoters that are active in green algae. The specification, however, fails to demonstrate that a nucleic acid molecule as set forth in claim 1 would be useful in obtaining a successful result from such a search.

According to the examiner (Answer, page 15), "the specification fails to disclose any characteristics of the corresponding promoter, or any other promoter within 'chromosome walking' distance; neither structural characteristics, by which the promoter might be identified, nor functional characteristics, by which a specific and substantial use for the promoter might be determined." By way of example, the examiner argues (Answer, bridging paragraph, pages 16-

⁹ In addition, we note the examiner's assertion (Answer, page 15), "[a]t the time the application had been filed, future experimentation on the part of one skilled in the art would have been required to determine which, if any, other plant species contained nucleic acid molecules that could have been obtained using the claimed invention, and under what experimental conditions."

17), assume

a nucleotide sequence is identified during the chromosome walk as a putative promoter by sequence analysis, is then subcloned into operable linkage with a reporter gene and transfected into an appropriate cell, but found not to express the reporter gene in the cells. This result could mean the putative promoter: is not truly a promoter, i.e. a false positive; is not the corresponding promoter; or is incomplete, i.e. lacked additional sequence elements required for promoter activity in the seed pod cells.

According to the examiner (Answer, page 11), appellants merely isolated the claimed nucleic acid molecule, “[t]hey have not tested, evaluated, or calibrated the claimed nucleotide sequence for any particular use.”

We recognize appellants' argument (Brief, page 9), “[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).” While we agree with appellants' statement, we fail to see how it applies to appellants' claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be “effective” at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is “refined and developed” to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful

as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Upon review of the record, we agree with the examiner that further experimentation would be required to use the claimed nucleic acid molecule "to detect the presence of and/or identify polymorphisms, as hybridization probes in an array for expression profiling, express proteins for generating antibodies, to screen for compounds to determine the effect of the compound on a population of green algae." Answer, bridging paragraph, pages 7-8.

As to the use of the claimed nucleic acid in microarrays (see e.g., Brief, page 6, n. 3), the examiner finds (Answer, bridging paragraph, pages 8-9), "[a]ppellants are not claiming microarrays or collections of nucleotides and the specification does not associate the claimed sequence with any trait of interest." According to the examiner (Answer, page 9),

[c]ontrary to [a]ppellants' assertions, further experimentation is required to identify a "real world use." For example, a negative hybridization result (which is already a further experimentation) to

such a screen tells what the nucleic acid is not and cannot be used for[;] and a positive result to such a screen requires even further experimentation to determine what, if anything, such a change means. Therefore, the claimed nucleic acid molecule does not provide an immediate benefit except providing a starting point for an artisan to further experiment in order to arrive at the point of immediate "real world" use.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. In regard to microarrays, we find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid molecule set forth in claim 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the specific information derived from a gene expression experiment would mean in the context of a nucleic acid molecule as set forth in claim 1.

To highlight the examiner's assertion (Answer, page 9), suppose, for example, that a researcher found that expression of the nucleic acid molecule set forth in claim 1 was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides

no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the nucleic acid molecule of claim 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use the specific gene expression data in the context of the nucleic acid molecule of claim 1.

Assuming arguendo, that a generic gene expression assay - one based on monitoring expression of thousands of uncharacterized nucleic acids - would

provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid - its data point - is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecule set forth in claim 1 is useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of claim 1 in such devices represents a substantial use.

Further, we understand appellants' position to be that a compound would be patentable if it was adequately described in the specification and was not disclosed or suggested in the prior art. This standard, however, is not the one set by Congress, which requires that a patentable invention also be useful and fully enabled, nor is it the standard that has been consistently applied by the courts.

Not only is appellants' proposed utility standard contrary to controlling case law, but there are reasons to expect that it would hurt – rather than help –

the microarray industry. Under appellants' standard, any naturally occurring gene, and fragments thereof, would be held to have patentable utility based on its use in generating expression data. The practical effect of this standard would be that making a microarray with, e.g., 1000 genes represented on it would require investigating the patent status of each oligonucleotide on the microarray. Not only that, but since appellants assert that their reasoning supports the utility of gene fragments, all of the subsequences of each of the genes would have to be checked to ensure that it was not the subject of someone else's patent.

For each of the genes (or fragments thereof) that was the subject of a patent claim held by someone else, a license would have to be negotiated – potentially thousands of such negotiations for the finished product. These transaction costs would have to be incurred for each new product that an aspiring microarray manufacturer wished to market. The industry gridlock likely to result from this scenario has been termed a "tragedy of the anticommons":¹⁰

By conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.

Heller, page 698.

¹⁰ Heller et al., "Can patents deter innovation? The anticommons in biomedical research," Science, Vol. 280, pp. 698-701 (1998). Available online at www.sciencemag.org/cgi/content/full/280/5364/698.

The Supreme Court has warned against allowing too many tollbooths on the road to innovation:

Patents . . . are meant to encourage invention by rewarding the inventor with the right, limited to a term of years fixed by the patent, to exclude others from the use of his invention. . . . But in rewarding useful invention, the "rights and welfare of the community must be fairly dealt with and effectually guarded." Kendall v. Winsor, 21 How. 322, 329 (1859).... To begin with, a genuine "invention" or "discovery" must be demonstrated "lest in the constant demand for new appliances the heavy hand of tribute be laid on each slight technological advance in an art."

Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230, 140 USPQ 524, 527 (1964).

We note that the examiner acknowledges appellants' assertion (Brief, page 6, n. 2), it "is irrelevant whether the corresponding mRNA or polypeptide have utility because [a]pplicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules." Answer, page 7. Nevertheless, the examiner asserts (Answer, bridging sentence, pages 8-9), "[t]he [B]rief does not dispute that no open reading frame (ORF), no encoded protein, nor any biological activity for the encoded protein has been disclosed for SEQ ID Number 1."

The basic guid pro quo of the patent system requires disclosure of an invention having substantial utility. On reflection, we find appellants' disclosure in this case does not provide a specific benefit in currently available form, and therefore lacks the substantial utility required by 35 U.S.C. § 101.

For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101. As discussed supra, claims 2 and 4-7 fall together with claim 1.

Enablement

According to the examiner (Answer, page 5), "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), "[t]he arguments stated above regarding ... [the rejection under 35 U.S.C. § 101]." Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph. As discussed supra, claims 2 and 4-7 fall together with claim 1.

Written description

The examiner rejected claims 1, 2 and 4-7 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, reasoning (Answer, pages 5-6) that

[c]laim 1 is directed to a nucleic acid molecule "that encodes an algal protein or fragment thereof comprising." The specification fails to describe any open reading frames, start/stop codons, or encoded proteins for SEQ ID Number 1. As such, these nucleic acid molecules are not described. At best, the SEQ ID Number may include a sequence encoding a fragment but not a full length protein.

The use of the term "comprising" is interpreted to encompass full length proteins and gene sequences that have not been disclosed or identified. The common structural features of these encoded plant proteins or fragments are not disclosed and thus the claimed subject matter cannot be considered as being described.

The specification describes only SEQ ID Number 1 and no longer sequences containing them. One can only envision the particular sequence disclosed and cannot envision any encoded protein sequence or larger sequences in which the claimed SEQ ID Number 1 is embedded.

As we understand it, the examiner's rejection has two bases. First, the claimed nucleic acids are not adequately described because the preamble of claim 1 states that the each of the nucleic acids "encodes an algal protein or fragment thereof," and the specification does not describe any encoded proteins.

We will not sustain the rejection on this basis. The claims are directed to nucleic acids, not proteins, and the specification describes the sequence of SEQ ID NO: 1, which defines the scope of the claimed nucleic acid molecule. In addition, as we have construed the claims, the phrase that the examiner objects to ("encodes an algal protein or fragment thereof") has no patentable weight because it merely recites an inherent property that is expected for the claimed nucleic acids, based on the method by which they were isolated.

The second basis of the rejection, as we understand it, is that because of the transitional phrase "comprising", the claims encompass a large genus of nucleic acid molecules, which are not adequately described by SEQ ID NO: 1 as recited in the claim. See the Examiner's Answer, pages 18-22. Apparently, the examiner is of the opinion that the claimed invention should be limited to SEQ ID NO: 1.

In response, Appellants argue that "[t]he fact that the claims at issue are intended to cover molecules that include the recited sequences joined with

additional sequences does not mean that [a]pplicants were any less in possession of the claimed nucleic acid molecules." Appeal Brief, page 16, footnote omitted.

We have interpreted the claims to allow for the addition of nucleotides or other molecules at either end of the nucleotide sequence set forth in SEQ ID NO: 1, but not to allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequence. See pages 3-4, supra. We agree with appellants that the claims, so interpreted, are supported by an adequate written description in the specification. The fact that the claimed nucleic acid molecules may have other molecules attached to either or both of their 5' or 3' ends does not diminish appellants' adequate written description of a nucleic acids molecule with the sequence set forth in SEQ ID NO: 1, as claimed.

Accordingly, we reverse the rejection of claims 1, 2 and 4-7 for lack of adequate written description.

SUMMARY

We affirm the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph.

We reverse the written description rejection under 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith)
William F. Smith)
Administrative Patent Judge)
Donald E. Adams) BOARD OF PATENT
Donald E. Adams)
Administrative Patent Judge) APPEALS AND
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